

# THE CROONIAN LECTURES ON LEPROSY RESEARCHES

BY

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## Lecture I. THE EPIDEMIOLOGY OF LEPROSY

When I had the great honour of being appointed to deliver the Croonian Lectures, I selected the subject of leprosy because I had spent my last few years in India in research on its treatment, and have since devoted several years to a study of its literature, while I believe it has not been discoursed on before this College since the late Dr. Robert Liveing delivered the Gulstonian Lectures in 1873, just when the epoch-making discovery of the lepra bacillus by Hansen was revolutionising our outlook on its etiology. Recent advances in treatment have at last furnished us with methods of dealing with the disease far more effectively than ever before, making the present time opportune for reviewing the whole subject. I propose in the first two lectures to deal with the epidemiology, mode of spread and prophylaxis of leprosy, and in the third to consider the improved methods of treatment.

### THE SPREAD OF LEPROSY OVER THE WORLD

Munro, in his learned articles in the *Edinburgh Medical Journal* of 1877-79, refers to an Egyptian record of 1350 B.C. of leprosy among negro slaves from the Sudan and Dafur, which is interesting in view of the present high leprosy rates in Central Africa, while very early records of India and China are believed to refer to leprosy. The first reliable records of its spread relate to the invasion of Europe through Greece about 350 B.C., probably by the armies of Darius, while those of Pompey carried it to Rome in 62 B.C. Galen mentions it in Germany in 180 B.C., and it spread all over Western Europe by the ninth century; both Sir James Y. Simpson and Sir George Newman

have recorded much interesting information regarding early leper hospitals in the British Isles, while Bergen had a leper hospital in 1266 and still has one to the present day.

Leprosy was, therefore, widely prevalent in Europe before the Crusades, but greatly increased from the eleventh to the thirteenth century, only to show a remarkable decline in the latter part of the fourteenth century. This, I believe, was partly owing to the Black Death of 1349, which is said to have carried off nearly half the population of Europe, for recent records show reductions of leprosy in Iceland and India due to epidemic disease and famines falling most heavily on outcast lepers; but also due, I feel sure, to the drastic segregation measures enforced in Western Europe during the Middle Ages; for, as Munro and others have pointed out, the disease only declined rapidly and eventually died out in just those countries where segregation measures were carried out, and lingers to this day in countries which neglected them, such as Scandinavia, the Iberian Peninsula, Russia, Turkey, and Greece.

While the disease was declining in Europe it was carried to the Western Hemisphere by the Spanish and Portuguese invaders, and later by the extensive negro slave trade from the very parts of Central Africa which still show the highest leprosy rates, and more recently still by Indian and Chinese immigrants. All the evidence goes to show that the aboriginal Indians were free from the disease, and those having little or no intercourse with leprous races from the old world still remain free to this day. As late as the middle of last century serious outbreaks of leprosy took place in several of the Pacific Islands, Hawaii having been infected by a Chinaman in 1848, according to Hildebrand, who saw the first indigenous cases five years later. The outbreak in New Caledonia was certainly due to a Chinese leper, who died about 1865 after living two years with a tribe, one of whom developed leprosy only a year later, and the disease spread so alarmingly that, according to Ortholon, within ten years from one-fourth to one-half the people in some places were attacked, while by 1910 no less than 90 per mille of the 8,000 convicts had become lepers. The epidemic soon spread to the neighbouring Loyalty Islands, the first case again being in a Chinaman affected in 1878, and by 1909 Nicholas found 35 per mille of the population to be lepers, although many cases were hidden. The



Marquesas Isles were next invaded, and by 1909 the leprosy rate had reached the appalling figure of 66·7 per mille (Buisson), or two hundred times that of India. Professor Jeanselme stated in 1903 that the Chinese had also 'carried leprosy to Indo-China, Siam, the Straits Settlements, Java, Sumatra, Borneo, the Philippines and other East Indian Islands, in several of which countries Chinese still form by far the majority of the infected,' Sir James Cantlie as early as 1897 having pointed out the rôle of the Chinese in spreading leprosy in these areas.

It is therefore clear that leprosy still retains its powers of spreading, and I fear there is good reason to believe that, with the opening up of communications and trade routes, the disease is now extending in tropical Africa, so that the problem remains a serious one for the British Empire. Thus the whole history of the spread of leprosy over the world is that of an insidious and slowly communicable disease carried by armies or the emigration of infected races to previously immune countries, leaving no doubt regarding the infectivity of the disease in some way or other, and of the necessity of safeguarding against its further extension.

#### THE WORLD DISTRIBUTION OF LEPROSY AND CLIMATIC CONDITIONS

The close relationship between hot, humid climates and high leprosy rates, which I demonstrated last year by maps illustrating the leprosy rates per mille throughout the world and in India, respectively, is the most important epidemiological feature of the disease, as the following brief summary will show. Every area with the very high rates of 5 per mille and upwards (that is, fifteen or more times the present rate in India, where leprosy cases can be seen daily in the streets of every town) is situated within the tropics, having high annual rainfall, usually of sixty inches or more, *e.g.*, a large part of tropical Central Africa, with such extreme rates as 20 to 60 per mille on the Ivory Coast, the Cameroons and part of Eastern Belgian Congo, these constituting the most severely affected large area in the world; while high rates are also met with in the hot damp countries of French and Dutch Guiana in South America, and in the Oceanic Islands, already mentioned as epidemically infected last century, and a few other areas.

In contrast with those high rates we have the remarkable fact that the only countries in the tropical zone, which have little or no leprosy, are the extremely dry areas of the Western Sahara, the French province of Mauretania, German South-west Africa, and the western coast of South America, all with less than ten inches of rain annually.

In the Northern Temperate Zone we also find the high leprosy rates of between 1 and 5 per mille in Norway and Iceland before active segregation measures were enforced, Japan and Korea, in all of which the rainfall is between 30 and 60 inches a year, against the usual rate for this zone of 10 to 30 inches.

Another important factor, however, comes into play in much of this zone, namely, the high degree of sanitary advance in Europe and North America greatly limiting the danger from returned emigrants infected with leprosy, with the result that the disease is no longer endemic in such countries.

The relationship between high humidity and relatively high leprosy rates and *vice versa* is illustrated in a most striking manner by my map of Indian leprosy distribution, rainfall and humidity data, the highest rates being met with in wet Burma, Assam, Bengal outside the deltaic region, Bihar, Orissa and the eastern Central Provinces, and the west coast of Bombay and Madras, which all have high monsoon rainfall, the leprosy rates in the Ganges valley actually decreasing with those of both the rainfall and the humidity in each division from east to west with the decreasing strength of the monsoon, while the humid Himalayan Kumaon Hills have ten times the leprosy rate of the hot, dry plains at their feet. On the contrary, the lowest leprosy rates are all met with in the dry North-western Punjab, North-west Frontier Province, Baluchistan and Sind, and in the dry central portion of the peninsula. The only exception is a somewhat high rate in comparatively dry Berar and the Deccan, probably due to infection by centuries of close trading with the people of the same race and language as those of the damp leprosy-infected western coast. Many other striking illustrations could be mentioned, such as higher leprosy rates in the rainy halves of Madagascar and Sumatra. I shall return later to the probable explanation of these facts.

### INVERSE RATIO BETWEEN LEPROSY PREVALENCE AND TUBERCULISATION

The remarkable relationship I found between damp heat and leprosy prevalence led me to collect data regarding tuberculosis in the tropics, and to study the writings on the subject of Colonel G. E. Bushnell and Professor Lyle Cummins. These showed that climate itself had much less influence on this disease than the degree of tuberculisaton of the population in any country, as illustrated by a high percentage of positive von Pirquet reactions indicating the numbers infected with mild or latent tubercle in childhood, protecting them to a large extent from the more acute forms of the disease in later life. It is now well established that native races in Central Africa, Oceana and America, among whom some of the highest leprosy rates are found, have very low percentages of positive tuberculin reactions, and are liable to suffer from decimating epidemics of very acute generalised tuberculosis on becoming infected from chronic cases of phthisis in Europeans. Thanks to Professor Calmette, von Pirquet reactions have been worked out in most of the French tropical possessions, and on studying these and other data I found that a low degree of tuberculisaton of the people occurred in just those areas where exceptionally high leprosy rates per mille have been recorded, as shown in Table I; intermediate rates are seen in such long tubercular infected countries as India and China, while the highest percentages of von Pirquet reactions are met with in Western Europe, from the greater part of which leprosy died out as an endemic disease over a century ago, in a manner which is unknown in any other part of the world.

In this connection it may be recalled that tuberculin gives reactions in leprosy, that such an acute observer as the late Sir Jonathan Hutchinson suspected that the tubercle bacillus may be modified by some element in badly cured fish to assume the power of producing leprosy, while such an eminent pathologist as the late Professor Sheridan in 1891 reported a case of leprosy with lung lesions in which he suggested the possibility ' that leprous lesions are the result of a *modified form of tuberculosis which tends to return to the normal type in the lungs.*' The italics are in the original. Although I do not for a moment endorse these views, they at least emphasise the close relationship of the two diseases, and suggest

as the most likely explanation of the interesting data in the table the possibility that infection by mild tubercle of a large proportion of a population may render it less susceptible to the infection of leprosy, this being one factor in the extinction of leprosy as an endemic disease in Western Europe, in addition to improved hygiene and other influences.

TABLE I  
Leprosy Rates per Mille and von Pirquet Reaction Percentages.

Country	Leprosy per Mille	Von Pirquet Percentages
France (Lille) ... ..	0.0	87.7
Austria ... ..	0.0	95.0
United States ... ..	Extremely low	94.9
Indo-China ... ..	0.67	48.0
Martinique ... ..	1.16	57.0
India ... ..	0.32	Fairly high
French Guinea ... ..	5.0	12.0
Senegambia ... ..	10.0	15.2
Tanganyika ... ..	7.0	21.0
Cameroons ... ..	20.3	4.4
Ivory Coast ... ..	60.7	8.4

However this may be, the reverse is certainly not the case, as it is well known that the most frequent fatal complication of advanced leprosy is pulmonary tuberculosis, and one which greatly complicates treatment, for doses of chaulmoogra oil derivatives which are of value in leprosy are actively harmful to the tubercular complication, although sodium morrhuate in small doses may sometimes be used with advantage in such cases.



NUMBER OF LEPERS IN THE WORLD AND IN THE  
BRITISH EMPIRE

Some ten years ago Dr. Victor G. Heiser estimated the world's lepers at 2,000,000, since when further data have come to light, especially regarding the great prevalence in Central Africa, and a close study has convinced me that 3,000,000 would be a more correct figure, including the following recorded data:—

In EUROPE 7,000, with about 1,000 each in South Russia, the Baltic Provinces and Crete, and about 500 each in Turkey, Roumania, Spain, and Portugal.

In ASIA 1,250,000, including 500,000 to 1,000,000 in China with its dense population, 102,000 in both Japan and India, 15,000 in both Indo-China and Siam, 5,000 in both the Philippines and in the East Indies, and smaller numbers in Malaya, Ceylon and Palestine, etc.

In AFRICA 500,000, nearly all in tropical Central Africa, although the estimate is only a very approximate one, the data being nearly all based on the percentages found in the examination of a few thousand persons in different areas. Other recorded data are Egypt 6,500, Madagascar 4,000, and South Africa 2,500.

In the WESTERN HEMISPHERE 30,000, including Brazil 15,000, Guiana 3,000, Cuba 1,500, the British West Indies 1,000, Colombia 6,500, Venezuela 750, etc., while Oceania has about 5,000.

All the above figures relate only to typical advanced cases, while considerable infected areas remain for which no data are available, and it is safe to say that there is at least one early unrecognised case for every recorded typical one, Muir's Indian experience leading him to think that even this is an underestimate. Yet the recorded figures total 1,792,000, so that, including early unrecognised cases, 3,000,000 is far from being an improbable number for the whole world, constituting leprosy a problem of unsurpassed difficulty and importance when the terrible nature of the disease is borne in mind.

Turning next to the number of lepers in British territories, I have entered the main data I have been able to collect from an examination of recent Colonial medical reports and other records in Table II, and although not complete, the total number comes in round figures to 156,000, two-thirds in India, and the greater part of the remaining

third in Africa, so that when allowance is made for an equal number of early unreported cases, there must be at least 300,000 lepers in our empire, the control of which is not the least of the white man's burden.

The important question, whether leprosy is increasing or decreasing, can best be studied by an examination of the following census returns of the number of lepers in British India during the last six decades, those of the British governed territories being selected, as this area, except for the small inclusion of Upper Burma, has remained unchanged since 1881.

CENSUS	...	1872	1881	1891	1901	1911	1921
LEPERS	...	101,590	118,953	110,509	85,878	92,433	85,122
PER MILLE	...	0·55	0·60	0·56	0·37	0·38	0·34

TABLE II  
Leprosy Incidence in the British Empire

Area	Year	Lepers	Per Mille	Remarks
India ... ..	1921 census	102,513	0·32	
Ceylon ... ..	1921	577	0·13	
Malay States ... ..	1921	450	0·34	In leper institutions
British N. Borneo ... ..	1919	54	...	In leper institutions
Fiji ... ..	1920	450	...	In leper institutions
West Indies ... ..	1921 census	1,189	0·74	
British Guiana ... ..	1921 "	247	0·83	
Cyprus ... ..	1921	74	0·23	In leper institutions
Africa :—				
Nigeria ... ..	1921 census	32,000	3·2	
Tanganyika ... ..	1921	7,026	0·7	1 in every 589 of population
Kenya ... ..	1922	2,018	0·74	6 in 8,067 persons examined
Uganda ... ..	...	? 3,000	1·0	303 lepers died in 1919
Nyasaland ... ..	1921 census	1,666	1·39	Reported to be spreading
S. Rhodesia ... ..	1921	1,000	1·11	Estimated at least 1,000
S. Africa ... ..	1923	2,501	0·46	In leper institutions
Mauritius ... ..	...	600	1·6	
Palestine ... ..	1902	600	0·86	Jeanselme

Unfortunately, the striking decline in the number and the rate per mille revealed in the figures of 1901 was almost entirely due to the issue of special directions excluding cases of leucoderma and syphilis, incorrectly returned as leprosy in the first three censuses, and so is not a real decline. A small part of the decline between 1891 and 1901 was due to a series of famine years, being followed by a slight increase in 1911, while the slight fall in 1921 was probably due to the influenza epidemic of 1918-19; so we may conclude that leprosy has been fairly stationary with a slight tendency to decrease during the last sixty years, during which prophylactic measures have been practically negligible. The scare that was raised about 1890 that leprosy was increasing rapidly in India, and which led to the appointment of the Indian Leprosy Commission in 1891, is, therefore, baseless as that Commission concluded, and there are good reasons for hoping that the more effective measures against the disease now available, if only they can be fully utilised, will lead to a decline of leprosy in India in the next few decades. Although the census figures have a relative value they only include the advanced, easily recognised cases, and Dr. Muir thinks the real numbers may be as high as between 500,000 and 1,000,000 if all the early cases are included, so it may be well to point out that the first result of the more general adoption of improved methods of treatment will be an apparent increase of leprosy, due to the early and more amenable cases coming forward from their hiding places and declaring their disease, instead of hiding it as long as possible. This is already evident in the Philippines, Hawaii and elsewhere, and so far from being a real increase, it will be the first promising sign of the possibility of controlling and eventually reducing the incidence of leprosy.

The AFRICAN problem is a still more difficult one, as the real numbers in our extensive territories are quite unknown, while the poverty and the small medical staffs compared with the population and extent of the countries greatly enhance the difficulty of dealing effectively with the disease. On the other hand, the smaller number of lepers in the West Indies, Malay States, Fiji and other smaller colonies afford more hopeful fields for continued efforts to reduce the disease by the methods to be described in the next lecture, when the prophylactic measures already in force in several of our colonies will also be dealt with.

## GENERAL CONDITIONS INFLUENCING THE PREVALENCE OF LEPROSY

Having now formed some idea of the prevalence of the disease throughout the world and in our empire, I next turn to a consideration of certain general conditions which materially influence the incidence and spread of leprosy, and require to be taken into account in devising prophylactic measures in different countries.

*Stage of Civilization and Hygiene.* One of the most potent general factors is the hygienic condition an infected race has reached ; this is well illustrated by the contrast between the conditions prevailing in Europe during the great prevalence of leprosy in the middle ages, as compared with the present time, when leprosy-infected Europeans returning from the tropics very rarely infect others under the advanced hygienic conditions in Western Europe within the temperate zone. The sanitary conditions under which the majority of the population of Great Britain dwelt during the eleventh to the fourteenth centuries cannot have been very far removed from those of the vast populations now living in one-roomed huts in India, China, Oceania and central Africa, where leprosy is now most prevalent. That such conditions are more potent than racial susceptibility to the disease is well shown by the reduction in the prevalence of leprosy, by improvement in their housing accommodation, among the large number of Scandinavian immigrants to Minnesota and neighbouring north-central states of America in the latter part of last century. Hansen himself visited the United States to trace the progress of leprosy among 170 Scandinavians, who had crossed the Atlantic from Norway when they were either already suffering from leprosy or developed the disease within the possible long incubation period after leaving their native country ; and he failed to find a single new infection in two generations, although leprosy continued to be prevalent among the same class in Norway itself. In explanation of this most interesting fact he pointed out that, whereas in their own country they had lived in such small and overcrowded houses that it was customary for all the males to sleep in one room and the females in another (as late as 1891, 42·4 per cent. of Norwegian town dwellings, according to Newsholme, having only one room), in Minnesota the immigrants built large houses, each man having his own bedroom, or at least his own bed,



thus greatly limiting the overcrowding which is such an important factor in furnishing opportunities for infection. The cool climate was also, doubtless, an important factor in addition to improved hygiene, for in the hot, humid, southern state of Louisiana, leprosy spread during the same period of last century among well-to-do French families, once more illustrating the influence of unfavourable climatic conditions. The effect of overcrowded one-roomed huts in favouring the spread of leprosy has also been pointed out by Green in Hawaii and Hearsay in Nyasaland.

Promiscuity both general and sexual, greatly favoured by overcrowding, is another most important factor in the spread of the disease, Buisson stating that the Marquesas Island epidemic was favoured by horrible sexual promiscuity ; the reports from Hawaii, where the women seldom knew who were the fathers of their children, laid great stress on the importance of the same factor, while more than one writer recorded that every European infected with leprosy was known to have had intimate relations with the native women ; Hillis reported the same occurrence in British Guiana and Drognaant-Landré in Surinam and Jamaica ; Sir George Newman mentions the unrestrained sexual relationships in the middle ages in our own country as having favoured the increase of leprosy. Even in recent times in the province of Galicia in Spain, the most unusual feature of a high leprosy rate among females was attributed by Tello to their promiscuous habits during the temporary emigration of their husbands.

Other favouring social conditions, to which the spread of leprosy has been attributed in Oceania and other tropical countries with a low degree of civilization, include eating out of the same dish and smoking a common pipe, while Hansen recorded that in Norway, during the frequent visits of the socially inclined people to relatives and friends, it was considered very bad form to object to sleeping in the same bed as a leper, unless he was in a very advanced stage of the disease.

Absence of all fear of leprosy favoured the spread of leprosy in Oceania and among the fatalistically inclined Mohamedans of Central Africa, as well as in Norway seventy years ago, before segregation measures had educated the people to realise the danger ; Munch pointed out the same thing in South Russia. On the contrary, various cruel customs among savage races have been recorded as

having reduced the incidence of leprosy in Senegal, the Ivory Coast, Nigeria, Madagascar before the arrival of the French, Nyasaland, Zululand, Sumatra, India and other countries.

Spread of leprosy by immigrants has already been mentioned in tracing the infection of America and Oceania, to which may be added the following instructive modern example in British territory. In 1863, for political reasons, leprosy-infected Hottentot tribes of West Griqualand were moved right across the Orange Free State to Griqualand East to the south of Natal, with the result that they infected both the country they passed through and their new headquarters at Kokstad, and the disease continued to spread among them until in 1895, 558 cases were known; the neighbouring Basutos also became infected, but partly through returned miners.

The escape of tribes having no intercourse with leprosy-infected neighbours is illustrated by the absence of leprosy to this day among the more remote American-Indian tribes of Brazil, Guiana and other South American countries; this is clearly not due to any lack of susceptibility to the disease, for Hillis recorded long ago that in British Guiana the Warara tribe, which alone had close relations with the infected negro population, including intimate relationships with some of the female inmates of the leper asylum in its early days when the administration was defective, did contract leprosy.

All the above epidemiological features of leprosy point to the disease being in some way or other a communicable one; during the latter half of the nineteenth century a great controversy raged on the subject, in which a Committee of this College played an important, but it is now clear, an unfortunate part, due to lack of knowledge in those pre-bacteriological days. As, in spite of the lepra bacillus having been discovered just over fifty years ago, the precise manner in which the organism passes from the diseased to infect the healthy is still not completely settled, many of the facts brought forward during those controversies are still of value in the elucidation of the problem. I believe, however, that no leprologist of repute any longer doubts that the disease is a communicable one, this having been universally admitted by all recent leprosy conferences, including the third international one at Strasbourg last year.

## CONTROVERSIES ON THE HEREDITARY AND CONTAGIONIST THEORIES OF LEPROSY CAUSATION

From the time of Moses right down through the middle ages, exaggerated views were held regarding the contagiousness of leprosy, doubtless due to the confusion with it of other more highly infectious skin diseases, and they resulted in the cruel segregation laws of those times. About the middle of the seventeenth century, when leprosy had nearly disappeared as an indigenous disease in Western Europe, the pendulum swung to the opposite extreme, and contagion was altogether denied; the spread of the disease was attributed solely to heredity, just as was the case with the closely allied tuberculosis, while leprosy was also described as a 'blood dyscrasia,' and these views were still nearly universally held down to the time of Hansen's discovery of the lepra bacillus in 1873, and even after that event were maintained by some authorities, although the infective theory steadily gained ground from that moment. The most influential supporters of the hereditary theory were the great Norwegian authorities, Danielssen and Boeck, who wrote the first accurate description of the nodular and anaesthetic types of leprosy in their book of 1848, in which they supported the hereditary theory with figures relating to 213 cases; these were for long accepted as proving their point, although when examined in the light of more recently discovered laws of heredity they have precisely the opposite bearing. The Norwegian authors regarded as proof of heredity the occurrence of two cases of leprosy within four generations of a family, even if the first case was in a grandchild and the second in a grandparent; this method of calculation showed direct descent in 32.4 per cent. and indirect in 54.5 per cent., the remaining 10.1 per cent. being attributed to spontaneous origin, the possibility of infection in a household or family being completely ignored, while their table showed more cases in the second and fourth than in the first and third generations, as well as more in the collateral than in the direct line of descent. These data are, therefore, in reality valueless as evidence of leprosy being essentially an hereditary disease. Later Norwegian authorities, including Hansen, opposed this theory, Holmsen, for example, finding only 12 out of 93 lepers whose parents or grandparents had suffered from the disease, and

no less than 11 of the 12 had been born before their parents or grandparents were attacked, while Munro, Vandyke Carter, J. C. White of the United States, Ehlers and other authorities might be quoted to the same effect.

Still more conclusive positive evidence against the hereditary view is afforded by the children of lepers being too few to allow of leprosy surviving more than two or three generations if it were solely hereditary ; this is shown by Munro, by Lewis and Cunningham, who found only five surviving children of 52 lepers in India, and by Arning in Hawaii, where the disease spread far too rapidly to be hereditary ; by the absence of hereditary transmission among the Scandinavian lepers in Minnesota and among many hundred children of lepers brought up by missions in India and elsewhere after early separation from their leper parents ; and by the infection of numerous Europeans in the tropics, whose ancestors had been free from leprosy for many generations. Virchow thought that only a predisposition to the disease was inherited, as was so long held with regard to tuberculosis, but I have found no evidence in recent medical literature in favour of that view. Nor is the question of purely academical importance, for the anticontagionist school argued that segregation of lepers must be useless because the disease is solely hereditary in origin.

*Hutchinson's Fish Theory.* The late Sir Jonathan Hutchinson's fish theory may conveniently be dealt with here, as it is also of pre-bacteriological origin, dating from 1863, in its first form. It held leprosy to be ' fish-eater's gout ' dependent on excessive consumption of badly preserved fish, but modified after the discovery of the lepra bacillus to mean that a particle of badly cured fish might produce leprosy developing many years later : a difficult event to disprove, although its author later admitted that his theory would not explain the spread of leprosy among non-fish eating Basutos. This fact led him to admit in addition ' commensal communication ' through eating food other than fish contaminated by a leper ; I do not know of any surviving supporter of the theory.



## THE COMMUNICABILITY OF LEPROSY

*Historical.* The history of the gradual re-establishment of the infectious theory of leprosy is an interesting one. In 1862, at the request of the Colonial Secretary, this College appointed a Committee to report on the infectiveness of leprosy. This Committee issued a bulky volume of evidence collected by means of a questionnaire from the Colonies and India, and concluded that leprosy was 'not contagious or communicable to healthy persons by proximity or contact with the disease,' but 'is essentially a constitutional disease indicative of a cachexia or depraved condition of the general system,' and that there was no evidence that 'would justify any measures for the compulsory segregation of lepers.' On the strength of this report the Colonial Secretary issued orders to repeal all laws in our possessions affecting the liberty of lepers (as the direct result of which, increases of leprosy have been recorded by Hillis in British Guiana, Munro in St. Kitts, Broes van Dort in the East Indies and Drognant-Landr  in Surinam), although, if Vandyke Carter's statement is correct, none of the College Committee had any material experience of leprosy, and Dr. N. C. MacNamara, a distinguished Indian Medical Service Officer, came to diametrically the opposite conclusion from a careful analysis of the evidence from India published by the Committee. This unfortunate report had one good effect, namely that it stimulated leprologists with experience in leprous tropical countries, such as Drognant-Landr  in 1869, Munro 1877, Brousse 1879, Hillis 1881, etc., to record convincing evidence of the communicability of leprosy. The last discordant note was sounded by the Indian Leprosy Committee of 1892, which appears to have been dominated by the ablest anti-contagionist leprologist of the day, Dr. Bevan Rake, nominated by this College, who reported that leprosy arose *de novo*, a view which was repudiated by the London Committee of the National Leprosy Fund who sent out the commission.

*Evidence of the Communicability of Leprosy.* The greatest difficulty in demonstrating the communicability of leprosy lies in the long incubation period, averaging several years, of the disease, which in many cases makes it impossible to trace the source of infection in endemic areas, aided by the insidious onset of the symptoms in

many cases and the tendency of patients to hide their disease. The following examples of the spread of the disease in newly infected areas, however, leave no room for doubt. In Louisiana a French woman developed leprosy in 1866, and within the next eleven years three of her four sons, one of two daughters, a nephew, an unrelated girl who nursed the mother, and an unrelated young man, who had frequently slept with the fourth infected son, all developed leprosy, although there were no other known cases in the country at the time ; the disease subsequently spread in the neighbourhood and remains to the present time. About the same time a French woman of Cape Breton Island of Western Canada, who was born opposite the Tracardie Leper Asylum of New Brunswick, developed leprosy at the age of 52, and within a few years five of her children, two of her grandchildren, a son-in-law, a man who attended the fourth infected son, and another man who was accustomed to sleep with the fourth infected son, all contracted leprosy when there were no other cases on the island ; all but the last case had died by 1881.

The carefully recorded Memel outbreak in East Prussia is equally instructive, for between 1848 and 1880 five Russian leper servant girls came to work in German families in this previously uninfected district, and by 1908 no less than 77 cases of leprosy had been traced directly or indirectly to these five original foci of infection ; the disease was still on the increase in 1899, infections nearly always occurring after long contact with a leper living in the same house. For example, four years after one of the Russian girls came to reside in a house, the father and his three children became lepers, and in a neighbouring friendly family the mother, three children, a female servant and the housewife's second husband were all attacked, and this second family infected the father, one son, two daughters, a daughter-in-law, a maid servant and two men servants of a third family, no less than 18 cases being thus traced to this one Russian leper girl.

*Frequency with which Infections can be traced.* In spite of all the difficulties in tracing the sources of infection of leprosy, Denny in the Philippines obtained histories of previous contact with leper relatives in 29 per cent., and McCoy in Hawaii and Gregory in Cape Colony in 37 per cent., although compulsory segregation laws made the patients loath to acknowledge infected relatives, while the percentages who acknowledged contact with lepers either relatives

or others were 60 per cent. in Dehio's South Russia cases and in Boyd and Warren's Texas series, 79.6 per cent. in Long's Basutoland, and 89 per cent. in Kereval's Caucasus cases; remarkably high figures under the circumstances, especially when it is remembered that unrecognised cases in an early stage of leprosy may sometimes be infective.

The most frequent sources and conditions of infection remain to be considered to complete this part of my subject. In this connection the relatives from whom infection is most frequently contracted may first be dealt with, the most significant facts being that in both the Philippines and Hawaii 84 to 85 per cent. of infections among relatives were those of children from parents or grandparents or from uncles or aunts, among brothers and sisters and between cousins, nearly all of whom are likely to be children and adolescents not over twenty years of age, while only 6 to 14 per cent. were older generations infected from younger ones, and the remaining 2 to 9 per cent. were conjugal infections: figures which confirm in a striking manner the evidence I shall adduce later to show that young persons are much more susceptible to leprosy than older people. Roumanian figures of infections from relatives show the same incidence, and also bring out the fact that in addition to 60 per cent. of infections of relatives, 5.5 per cent. were house infections of others such as servants, and the remaining 30 per cent. were due to other close associations.

The proportion of healthy persons living with lepers who become infected has also been investigated with very close agreement among the investigators shown by the fact that the data recorded by McCoy in Hawaii, Gregory in Cape Colony and by the Indian Leprosy Commission are respectively 4.2, 4.5, and 5.5 per cent. while in Japan and in Norway the figure in both cases was 2.7 per cent. The percentage of infections among conjugal couples are very similar, varying from 2.6 in Cape Colony, 3.8 in Japan and Norway, to 5 in Basutoland, 5.1 for males and 4.8 for females in Hawaii and 6.5 per cent. in India. Thus in both cases only about one in twenty of persons living in close association with a leper contract the disease, showing that leprosy is far from being a highly contagious disease; in fact probably not more so than tuberculosis itself under very similar conditions.

Further light on the subject is shown by a study I have made of

700 cases, in which the probable source of infection was traced and recorded in the literature of the last sixty or seventy years; an analysis of these I have already published and it may be summarised here:—

In 12·14 conjugal infection, and in 6·14 cohabitation, or 18·28 per cent. In 25·7 house infection, in 5·0 room and in 9·14 bed infection, or 39·84 per cent. Infection due to attending on a leper occurred in 19·87 per cent. Close association in 16·14, and from a leper playmate in 3·28 or 19·42 per cent. From wetnurse 1·14 per cent., wearing a leper's clothes 0·43 per cent., vaccination 0·59 per cent. and inoculation from a leper in 0·43 per cent. completes the total.

In view of the old anti-contagionist arguments that infection rarely resulted from conjugal relationship or from attending on lepers, it is interesting to note that almost one-fifth of my collected cases fell under each of these headings. Further, if the bed infections are added to those due to conjugal or cohabiting relationship nearly 30 per cent. of the infections occurred after sleeping in the same bed with a leper, while as most of the cases of attending lepers were among those nursing private cases in the patient's house, if we add a little over half of those cases due to attendance to the conjugal and house infections, we find that at least 70 per cent. of the infections took place as the result of living in the same house with a leper, usually for a considerable time: once more emphasizing the fact that long and close contact with a leper commonly precedes infection and that it is essentially a house infection, yet again bringing out a closely parallel condition with tuberculosis.

Although long and close association usually precedes infection, very short contact may suffice, three cases being on record in which young Europeans in the tropics developed leprosy within ten months to two years after cohabiting with a leper woman on a single occasion, at least one of them being under the influence of alcohol at the time. It is interesting to note that in Nigeria, Madagascar and China, native opinion firmly believes in leprosy being contracted by sexual intercourse, while lepra bacilli have been found in the semen, in lesions of the penis and vulva in lepers; the greater frequency of leprosy among males and at the age of adolescence might be explained by infection during such close relationships, although not necessarily directly as in venereal disease, as the frequency of



the discharge of innumerable lepra bacilli from the nose may be an important source of infection.

Numerous further examples of house infections might be given, the danger from leper servants for example, as shown by the Memel cases, and confirmed by Landré's 12 cases of pure European children being infected from leper servants. In well managed leper asylums the danger to attendants is almost negligible, but in the early days of the Molokai settlement of Hawaii with very defective administration, no less than 16.4 per cent. of infections among 244 healthy attendants were detected within three years, chiefly contracted through intimacy with the leper females. Doctors have occasionally become infected, sometimes through gross carelessness and neglect of ordinary cleanliness. Although in so many cases the probable source of infection can be traced, yet occasionally a European living under the most favourable hygienic conditions is mysteriously infected, possibly through clothes infected during washing or other unsuspected or indirect contact with a leper, such inexplicable cases in Europeans under very favourable hygienic conditions in India having come within my knowledge, so that no one can be considered quite safe while living in a leprosy endemic area, however slight the risk may be.

The greater infectivity of the nodular type of leprosy is another important factor which is still too little recognised in prophylaxis, although well known to experienced leprologists. It is due to the copious discharge of lepra bacilli from ulcerated nodules and from nasal lesions in about 80 per cent., while in the anaesthetic form the bacilli cannot escape from the nerve trunks and are only discharged in the nasal mucus of 6 to 15 per cent.; in advanced chronic nerve cases the bacillary infection often dies out with loss of all infectivity, but not until permanent crippling has resulted. These cases sometimes constitute 75 per cent. of leper asylum cases in India and elsewhere, their isolation being of little prophylactic value. This difference in infectivity is well brought out by the analysis of my 700 collected cases, for in 113 of them the type of the infective case was recorded, and in no less than 94.7 per cent. they were nodular, and only the remaining 5.3 per cent., or one-twentieth, were of the anaesthetic type. In Norway special care was rightly taken to isolate as many as possible of the infective nodular cases,

while only last year the 2,501 lepers in the South African asylums were examined from this point of view and no less than 693, or 28 per cent., were released as uninfected, thus providing valuable accommodation for infective cases.

*Age susceptibility of leprosy* is an equally important point, which may be illustrated by the figures of over 4,000 cases in which the age at the probable date of infection, or on the first appearance of symptoms (from which the average incubation period of three to five years must be deducted), was recorded by different observers. An analysis shows that infection took place within the first 20 years of life in 50 per cent., by 25 years of age in 66 and by 30 years of age in 75 per cent., after which the susceptibility is greatly decreased.

The great susceptibility of children to leprosy is well brought out by Denny's Cullion figures and the 1922 data from the same place, showing that no less than 44 per cent. and 33 per cent. respectively of the children of leper parents living with and brought up by them became infected with leprosy; Mouritz reported 34.6 per cent. of similar infections in Hawaii, while Drs. Lie and Sand of Norway recorded that among 2,010 children of 587 couples, 7 per cent. became infected when the father alone was a leper, 14 per cent. from the mother alone, and 26 per cent. when both parents were lepers, the infection of children exposed to infection thus being five to nine times as frequent as among conjugal couples. As all the evidence goes to show that leprosy is extremely rarely, if ever, congenital, the importance of separating healthy children from their leper parents from birth cannot be exaggerated; a case has recently been reported in which a child removed from leper parents two months after birth developed the disease three years later, although, fortunately, such early infections are very rare.

I have now completed my survey of the distribution, epidemiology and of the various factors influencing the spread and infection of leprosy, and cleared the ground for considering the mode of infection and prophylaxis of the disease in my next lecture.

## Lecture II. MODE OF INFECTION AND PROPHYLAXIS OF LEPROSY

Fifty years ago Hansen discovered the lepra bacillus, which is now generally accepted as the cause of the disease. The precise manner in which the organism gains access to the human system is still unproved, owing to the failure to discover reliable methods of cultivating it or of infecting animals with the disease, and the equivocal results of attempts to infect man himself, Arning's positive result in Hawaii of inoculation of a convict having been invalidated by opportunities this man had of being infected from leprous relatives. In the case of rat leprosy, due to another acid-fast bacillus, however, Professor Marchoux has shown that the disease is inoculable, and it may be said at once that there is a remarkable consensus of opinion among experienced leprologists that human leprosy is also conveyed by inoculation of the organism through the skin or the nasal mucous membrane ; but as proof is wanting, it is necessary to consider the indirect evidence bearing on the probable mode of infection of the disease, and it was for this reason that I dealt so fully with the epidemiology of leprosy in the first lecture.

### POSSIBLE MODES OF INFECTION

Inhalation has for long been regarded as the common mode of infection of pulmonary tuberculosis, although the work of Calmette has thrown grave doubt on its frequency. In leprosy the lung is very rarely affected and never primarily as far as I know, while Muir has found that the lung lesions respond to treatment more rapidly than the skin ones. There is thus no evidence that inhalation is a common mode of infection in leprosy.

Infection through the ingestion of food was thought to be possible by Hutchinson, but I can find no valid support for this view in medical literature, although it is difficult to exclude the possibility of the lepra bacillus passing through the gastro-intestinal mucous membrane and lymphatic glands to reach the blood stream without leaving any visible trace of its passage, however unlikely this hypothesis may be. Moreover, the incidence of leprosy in households rarely shows several members developing the disease at about the same

time, as in food infections, the cases being nearly always separated by a year or more, as if due to separate accidental infections by another route.

Inoculation through the skin, on the other hand, has been thought to be the common mode of infection in leprosy by such authorities as Vandyke Carter as early as 1867, Hansen and Looft, Kaposi, Munro, White, Besnier, Hillis, Mouritz in Hawaii, Tonkin of Africa and many others. The only difficulty in marshalling the evidence in favour of this view is to select from the innumerable records bearing on it, of which the following are some of the most striking.

Hillebrand reported the infection of a European child in Borneo, who thrust a thorn into his flesh immediately after a native leper boy had inserted it into his own flesh ; and Solano met with a similar case in Colombia, in which a boy aged six thrust needles into his flesh immediately after a negro leper playmate aged eight had introduced them into nodules on his limbs, with the result that the first boy soon after began to get febrile attacks and pains in his limbs, and one year later was covered with a typical tubercular leprotic eruption. These two cases are of especial significance in view of the subjects being children of a highly susceptible age, whereas all the negative experimental inoculations I have found recorded were in far less susceptible adults, none of those inoculated by Profeta having been under 25, while the majority were over 30 years of age, when susceptibility is small.

Even more conclusive are the following two cases of doctors inoculated while operating on lepers. Dr. Ehlers reported the case of a Danish doctor in the West Indies, who wounded a finger during an obstetrical operation on a leper negress ; the wound healed slowly and he soon after developed in the injured finger severe pains, which later proved to be due to anaesthetic leprosy ; in Hundadze's case a medical man inoculated a wound of his right finger in opening a leper's abscess ; the wound healed normally, but two months after the site of the wound became red and swollen, this symptom being accompanied by fever for three days, and three weeks later red leprosy patches appeared on the injured finger ; these were at first taken to be syphilis, but proved to be leprosy, leaving no doubt of infection through the wound. Hatch in Bombay has recorded a case of anaesthetic leprosy of the ulnar nerve closely



following a wound made while doing a post mortem on a typical leper, the diagnosis being confirmed by Vandyke Carter.

These cases, among others which might be quoted, should suffice to establish the possibility of leprosy being inoculated through the skin, while the close resemblance between limited dermal leprosy and tubercular dermatitis, now generally accepted as due to inoculation with the tubercle bacillus, presents an interesting analogy in a closely allied organism.

Vaccination as a possible cause of leprosy has given rise to much controversy and some loose statements, but very suggestive facts are on record; the possibility of its occurrence receives strong support from Arning's observations in Hawaii, proving that lepra bacilli were frequently present in vaccine lymph taken from apparently healthy skin in persons with extensive cutaneous leprosy, but not in vaccine from purely nerve cases, and he considered that there was strong evidence that leprosy had been spread in certain parts of Hawaii by carelessly performed arm to arm vaccination. Cases highly suggestive of infection in this manner have been recorded by Hillis, Gairdner of Glasgow and others, but as they occurred in endemic areas other modes of infection cannot be excluded; it is, however, of interest to note that Gavin Milroy records that Creole families of the West Indies obtained their lymph from the United States for fear of leprosy. Quite recently new light has been thrown on the subject by the observations of O. E. Denny and R. Hopkins at the United States Leprosarium, where after vaccination of both the healthy staff and the lepers, the latter alone had severe reactions; in eleven of them local swelling, fever and the appearance of fresh nodules and even ulnar neuritis appeared; so that it is possible that such reactions in early unrecognised or latent cases of leprosy may formerly, in Hawaii and elsewhere, have been taken for infections due to vaccination. In any case, infections clearly due to vaccination in leprosy countries by the old arm to arm method can have very rarely resulted, while they are impossible with the general use of calf lymph at the present time.

Infection from clothes and bedding has frequently been suspected, Tonkin regarding this as a common occurrence in badly infected Central Africa from Nigeria to the Sudan, where it is the custom for clothes to be passed down, without ever being washed, from the

rich to the poorest until worn out ; to the sleeping of whole families together on mats in Hawaii, India and elsewhere have been attributed inoculations over the buttocks, shoulder-blades and cheeks ; a case of a primary lesion in the last position in a child, who slept on the bed of a leper relation, having recently been reported by Muir in Calcutta ; wearing lepers' clothes has also been recorded as a cause of infection in the West Indies and Norway, etc., while in Riga a large proportion of the few lepers occurred among washerwomen : all indicating possible infection through inoculation from clothes or bedding soiled with leprous discharges containing enormous numbers of bacilli.

Sites of primary lesions as evidence of inoculation afford further important evidence, the especial frequency of anaesthetic leprosy in bare-footed races having been recorded in Abyssinia, where ten out of twelve lepers are said to be of this type, the Sudan, Hawaii, Crete, Java (with 50 per cent. of such cases according to Gell), Peru and India. Only last year Muir published diagrams of the distribution on the surface of the body of the first noticed lesion (most of which are considered to be the probable primary sites of inoculation), of no less than 1,056 lepers in Indian asylums and noted that they greatly predominated on exposed parts, such as the face, and extensor surfaces of the extremities, as well as over the buttocks and shoulder-blades exposed to friction on bedding and sleeping mats. Further, in two areas on alluvial soil, primary lesions on the feet were very uncommon, but in two separate hilly and stony districts among the bare-footed they were frequent on the feet ; all facts indicating inoculation through the skin as the most usual mode of infection.

Inoculation through the nasal mucous membrane is another possible mode of infection first pointed out by Professor Jeanselme in 1897 and supported by Stricker, Muir and others, but recent examinations of a number of children of lepers in the Philippines for early signs of the disease showed none in which the nasal mucous membrane was infected without skin lesions, although the opposite occurrence was common, so that primary nasal infection is probably much less frequent than that through the skin.

The rôle of insects in the transmission of leprosy has received much investigation in recent years without any one insect being especially incriminated. Flies can carry numerous lepra bacilli

from ulcerated skin lesions to the skins of neighbours or to food, indicating the advisability of putting a stop to markets being frequented by begging lepers as is so frequent in the East. Acid-fast lepra-like bacilli have also been detected in the alimentary canals or faeces of insects fed on lepers, as shown by the following recorded data :—Bed bugs have yielded positive results in 9.9 per cent. of 302 bugs fed on lepers, and in one per cent. of those caught on them, while E. C. Long has recorded the development of leprosy in a man in South Africa within a year of his having slept in a bug-infested hut recently vacated by a leper, although he had never lived in a house with one. With a single exception investigators have found under one per cent. of mosquitos fed on lepers to harbour the bacilli. The *Acarus scabiei* of itch has been suspected by Heiser and by Mugliston to play a part in leprosy infection, while lice have also been accused.

*Explanation of Relation between Humidity and Leprosy.* I may now return to the relation between high humidity and temperature and leprosy rates which I showed in the first lecture, and for which I have suggested the following explanation. In the first place, as the leprosy bacillus has not yet been cultivated with certainty, it presumably lives but a short time outside the human body in the absence of any known animal or insect carrier, so that the absence of leprosy in very dry, hot countries may be explained by those conditions being most unfavourable for the extracorporeal survival of the leprosy bacillus; while in hot, damp climates it will find more favourable conditions, especially if it gets on to the skins of neighbours of an infective leper. Such climates also greatly favour insect life, while the frequency of the first noticed lesions on the exposed parts of the body and extremities is easily explained on the ground that they are subject to frequent insect bites, affording minute lesions in the skin through which the lepra bacilli may gain access to the dermal connective tissues and nerve endings so favourable for their multiplication; the presence of humidity and numerous insects thus favour infections from lepers living in the same house or in close association with the healthy, these being, as I showed in the last lecture, the essential conditions under which the disease spreads. Such an explanation also affords a good basis for the study of prophylactic measures, to which I must now turn.

## THE PROPHYLAXIS OF LEPROSY

Hitherto, the prophylaxis of leprosy has practically been summed up in the one word segregation. The first isolation laws are probably those of Moses ; drastic measures were enforced in the middle ages in Europe, including deprivation of civil rights, divorce, isolation in leper houses, wearing a special garb, prohibition of entry into inns, churches and bakehouses, touching or giving anything to children, washing in common fountains, eating or drinking with any but a leper, speaking in the streets except in a whisper, etc. ; all highly effective measures against a disease now known to be rarely acquired except by prolonged close contact with a leper. It is not of the highly contagious nature it was thought to be in ancient times and by some savage races to-day, who are recorded to have tried to control leprosy by killing all young lepers in Nigeria, or all ulcerated ones as in Nyasaland and Fiji, burning them alive in Sumatra, drowning them in Western India, etc. Isolation of advanced lepers in special villages has been reported from Central Africa, Madagascar, Indo-China, China and parts of India such as the Garo Hills in Assam, while even in Spain lepers are said to be driven into the mountains and deserts : so great is the fear of this mutilating and disfiguring disease, which still allows of severe segregation measures necessitating life-long isolation in most cases, being sanctioned by public opinion, such as would not be tolerated against other diseases with such a protracted course. The whole policy of segregation against leprosy requires careful reconsideration in the light of our present knowledge of its epidemiology, as a preliminary to which the results hitherto obtained by the measure must first be reviewed, beginning with those under the most favourable conditions in European races in the temperate zone.

*The Norwegian System.* As the greatest obstacle to segregation is the natural tendency of the sufferers to hide their affliction, the essence of the humane Norway system of segregation is to provide comfortable hospital conditions to attract the lepers, and to resort to compulsion as little as possible, that measure only being applied to indigents during the early years. In 1856, when the measures were commenced, there was good reason to believe that leprosy was increasing in the country, 2,833 cases then existing, or 1.91 per mille, six times the present official rate in India, and



only 235, or 8.3 per cent. were in leper institutions. Careful records were kept, while newly discovered cases were entered in the year in which their symptoms appeared, and after a time Hansen and Looft were able to report that the decrease in different districts was in proportion to the numbers isolated, and that the new cases arising in any area were in proportion to the number of unisolated nodular infective cases forming foci of infection. Owing to the favourable results obtained, the laws were strengthened in 1878 and again in 1885, when all lepers were isolated at public expense, and local authorities had power to remove lepers from their houses, unless they could be isolated at home under satisfactory conditions and close supervision. The results are shown in Fig. 1, which I have

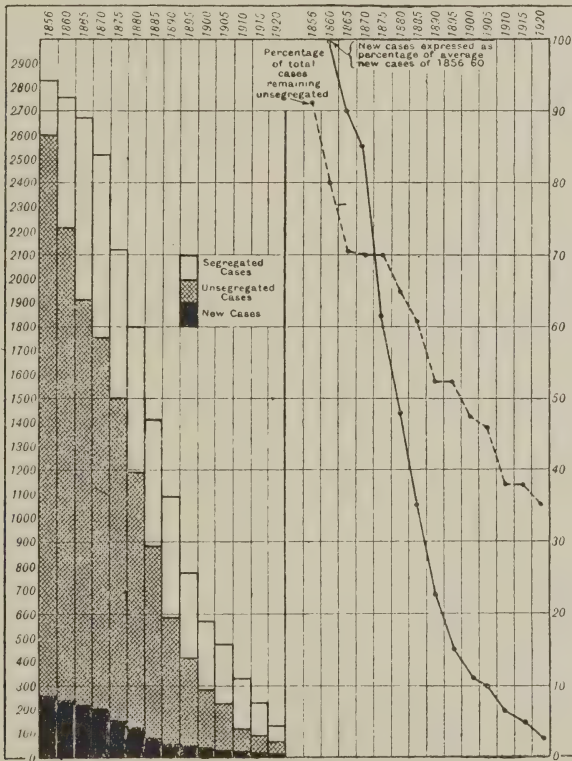


FIG. 1. Chart illustrating segregation in Norway.

prepared from the official figures, the latest having been kindly supplied to me by Dr. H. P. Lie (who succeeded Dr. Hansen in

charge of the work), the average number of new cases, and of the segregated and unsegregated being shown for each five-yearly period, while to the left the curves of the percentage of new cases, as compared with the average number from 1856-1860, and the percentage of unsegregated lepers in each five years are also given, showing a reduction of the total cases to 160 in 1920, while in 1923 there were only 140, or 5 per cent. of the original number in 1916-20; the new cases were only 2.7 per cent. of those in 1856-60, although it was not until after 1890 that over half the total lepers were isolated, these cases, however, including a much larger proportion of the infective nodular types. An interesting feature of the Norway experience was that five out of six of the newly-discovered cases dated their first symptoms back for three or more years, during which they had opportunities of infecting their households before they were discovered and isolated (a difficulty which is still greater among backward tropical races), and it accounts for the slow, if sure, effects of the measure, which is one of the most successful yet recorded, and clearly establishes the value of efficient segregation where it is practicable.

In SWEDEN compulsory notification and the provision of hospital accommodation in the affected central Helsingland and Dalecarlia districts led to a fall from the maximum number of 103 cases in 1873 to 89 in 1907 and 37 by 1923, a reduction of 65 per cent., the provision of comfortable conditions in the leper institution enabling a high proportion of the cases to be isolated without compulsion.

In ICELAND there were 226 cases, or 3 per mille in 1896; the leper hospitals, which had been closed in 1848 on account of the non-contagionist views of Danielssen, were reopened through Dr. Ehlers' influence in 1897, who also got a law passed prohibiting children under fifteen years living in the same house with a leper—a measure which would be of great value in this country if it could be applied to open infectious cases of tuberculosis. The result was that leprosy declined to 67 cases and 0.78 per mille by 1920, or just one-fourth of the rate twenty-four years before, fully justifying the steps taken. I am indebted to Professor Monrad-Krohn of Christiania for the recent figures of these three countries.

In MEMEL compulsory segregation and search for contacts were enforced in 1893, when there were 25 cases and the disease was still

increasing ; a decrease set in in 1898, by 1908 only 15 controlled cases remained, and by 1914 the outbreak had been stamped out : these results confirm the value of humanely conducted segregation in European countries. Further, in the New Brunswick province of Eastern Canada an old endemic focus dating from 1815 among the French was controlled, with the aid of the Catholic priests, by a voluntary system of isolation, and the cases slowly decreased from a yearly average of 32 in 1875-79 to 20 in 1910-14, and with more active measures fell to 12 in 1920-22, including a few from other parts of Canada.

*Segregation in the Sub-Tropical Zone, 40° to 23½° F.* In countries of this zone with moderate temperature and rainfall, leprosy rates are mostly low. CYPRUS in 1878 had over 150 known lepers ; in 1891, compulsory notification and segregation were introduced ; in 1901, there were 125 cases, 0.57 per mille, and in 1921 only 74, or 0.23 per mille, a decline of 60 per cent. The 1921 report states that there is now 'a good prospect of stamping out the disease in Cyprus before very long.'

The AUSTRALIAN COMMONWEALTH mostly falls in this zone, except the north of Queensland and the little-inhabited north coast, and compulsory segregation has been enforced for some time ; leprosy Chinese and Oceanic islanders are repatriated, Europeans being retained until bacteriologically free for several years. Queensland had 78 lepers in 1910 and 50 in 1921, while New South Wales has had from 24 to 20 with a yearly average admission of three during the last fifteen years up to 1922 ; the remaining colonies have only isolated cases. A single institution might well care for all the cases in the Commonwealth.

SOUTH AFRICA presents a much more difficult problem with its large native population, and records of the admissions to the Robben Island settlement since 1845 show 20 to 30 yearly up to 1886, while immediately after the introduction of compulsory segregation in 1892 the yearly admissions rose to 294, and averaged 107 from 1894 to 1905 ; as late as 1907, Mackie reported that only 23 per cent. of the lepers registered that year could be accommodated in the asylums, and the recorded rates per mille for Cape Colony rose from 0.41 in 1891 and 1.02 in 1895 to 2.21 in 1907, clearly showing that in the absence of efficiently enforced segregation the disease was slowly increasing.

Recently the Union of South Africa has provided additional accommodation, and in 1923 there were 2,501 lepers isolated in several asylums, including the 693 bacteriologically negative cases since released as uninfected. In Basutoland, Long reports that the spread of the disease has been controlled by the active segregation measures enforced there in recent years.

*Segregation in Tropical Countries.* Still greater difficulties are met with in humid tropical countries with backward populations, although in some restricted areas with small numbers of lepers, promising results have occasionally been obtained; these are best illustrated by the WEST INDIAN data I recently collected from the colonial reports, which are of especial interest,—the colonies who did not carry out segregation furnishing admirable controls, as shown by the following data:—

Jamaica began segregation in 1896. In 1891, there were 450 lepers, 1.23 per mille, and in 1921 only 319, 0.35 per mille, a decrease in twenty years of 52 per cent.

British Guiana began segregation in 1905. In 1891 there were 353 lepers, 1.23 per mille, and in 1921, 247, 0.83 per mille, a decrease of 42 per cent.

Trinidad only began segregation in 1915. Lepers in 1871 numbered 102, 0.93 per mille; in 1891, 225, 1.12, and in 1921, 526, 1.50, an increase of 81 per cent.

Barbadoes had no segregation up to 1922. Lepers in 1901, 230, or 1.21 per mille, and in 1921, 164, 1.05 per mille, an increase of 48 per cent.

St. Kitts, with no segregation, had 112 lepers, 2.44 per mille in 1891 and 100, 2.60 per mille.

Of the smaller islands St. Lucia and Granada, without segregation, showed no change in the leprosy rate per mille, while St. Vincent, with segregation of indigent lepers, showed a decrease from 57 in 1881 to 30 in 1911 and 19 in 1921.

Thus all the colonies who relied on voluntary isolation in asylums of a few advanced cases showed either an increasing number of lepers or a stationary condition, while the island colonies which carried out compulsory segregation showed a great reduction within two or three decades; thus affording a striking object lesson to other colonies.



FIJI commenced compulsory segregation in 1911 on an island settlement, where the numbers isolated increased from 40 in 1911 to 351 in 1920, and are now being treated efficiently by Dr. Harper, but it is too early to judge of the effects of these measures. Penrhyn Island has partial segregation, and only 27 cases in seventeen years. In the MALAY STATES a Leprosy Prevention Ordinance was passed in 1893 and leper asylums were gradually opened; the average yearly admission increased steadily from 150 in 1895-1901 to 174 in 1912-16, but fell to 152 in the five years up to 1921, indicating that a decline of the disease has now set in. CEYLON passed a leper ordinance in 1901, but deficient accommodation has prevented its efficient enforcement.

In our TROPICAL AFRICAN COLONIES, lack of funds has prevented anything material being done, except in Tanganyika, where there are 39 leper villages with land to cultivate, making many of them self-supporting.

In MADAGASCAR many lepers are isolated in settlements under missionary care, but I have not been able to get any information on the results yet obtained.

Two important trials of segregation in backward tropical areas under most difficult conditions remain to be considered, as they have important lessons.

In HAWAII, as early as 1865, a leper hospital was opened near Honolulu for the treatment of the earlier cases, and the famous leper settlement where Father Damien fell a victim to the disease after many years of invaluable work, was formed on the Molokai peninsula; but in spite of an expenditure of 4 per cent. of the total Island revenues the conditions were bad, resulting in the inevitable hiding of cases as long as possible, so that over 90 per cent. were of several years' standing when first discovered. Moreover, political influences caused great variations in the enforcement of the law, and very little effect was produced on the prevalence of leprosy, until in 1891, American influence greatly improved the conditions, since which the rate per mille has fallen from 13.5 in 1890 to 2.16 in 1919; during the last few years effective treatment has been introduced with favourable results, which I shall deal with in the next lecture.

In the PHILIPPINES the Americans, under Dr. Victor G. Heiser, inaugurated, under difficulties, a great effort by means of compulsory

segregation to stamp out leprosy, and opened the Culion settlement in 1906, regarding the results of which contradictory statements have been published. Thanks to the kindness of Dr. H. W. Wade, chief medical officer, in supplying me with the official figures to date, I have been able to work out Fig. 2, the upper curve of which shows the yearly (continued line) and three-yearly (broken line) average admissions, while the lower curve shows the yearly total Culion lepers (continued line) and the average three-yearly number corrected to the average mortality of the whole period (broken line).

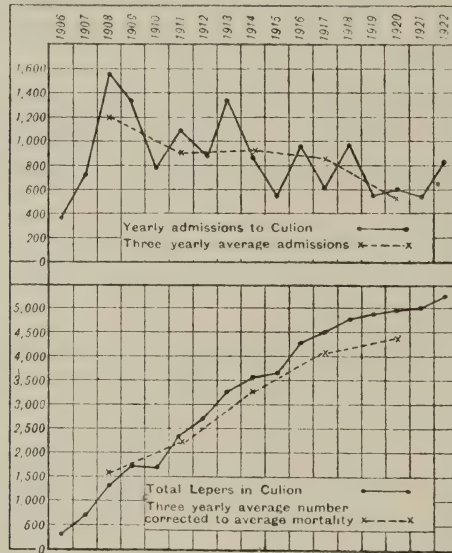


FIG. 2. Chart illustrating the result of segregation in the Philippines.

The admissions naturally show the highest rate in the first three years after the opening of the settlement, the second three years show a steady rate, the third a slight fall, and the three years 1919-21 a marked fall in the admissions, while 1922 shows a rise due to the satisfactory reason that numerous lepers voluntarily declared themselves to obtain the benefit of the improved treatment now available. The lower curve shows that the total number in the colony is still rising, although at a gradually less rapid rate, the flattening-out of the curve being especially marked for the years 1918-21, indicating that the peak of the curve was nearly reached, apart from the new factor introduced by the attractive power of the

new treatment. In view of the comparatively short duration of the measure, and the immense difficulties in collecting the lepers from the numerous islands of the Philippine group, this result cannot be considered unsatisfactory, although not coming up to the sanguine expectations with which it was started, and with the assistance of the American doctors now applying the improved treatment, still better results are likely to accrue within the next decade or two.

*Failures of Segregation and their causes.* In addition to the foregoing examples, many failures of attempted segregation are on record, which have their lessons, and they may most conveniently be classified in accordance with the causes of their lack of success.

Perhaps the most common cause of failure is vacillating policy, such as in French Guiana, where between 1823 and 1891 no less than twenty administrative alterations in policy were promulgated, rendering continuous application of efficient measures impossible; Hillis and Neal record very similar conditions in British Guiana. In New Caledonia, the French first ineffectively tried isolation of the lepers in five villages, later in a central asylum on Art Island, which had to be given up for financial reasons, and then reverted to forty-two small leper villages, which failed owing to lack of authority of the native chiefs, although in the Marquesas Isles this plan is said to have been successful with the aid of gendarmes. Political influences prevented effective enforcement of leper laws in Louisiana and Algeria as well as at first in Hawaii.

Defective administration has been another frequent cause of failure, the worst instance of which is probably that of Crete, where Ehlers showed that under Turkish authorities the leper occupants of the four leper villages outside the four main towns not only begged in the cities, but the more successful of them bought their houses in the leper villages, and then let them to healthy persons while they went on begging tours through the island, and some of those who took their houses contracted leprosy; the so-called segregation being in reality an ideal method for spreading the disease: yet Hutchinson quoted this as an example of the failure of segregation. Deficient accommodation, such as obtained a few years ago in South Africa, also comes under this heading.

These examples will suffice to show the great difficulties encountered in enforcing efficient segregation in many tropical countries,

mainly due to the impossibility of discovering and isolating the earlier cases as long as we have no effective treatment of the disease. Moreover, the numbers of lepers in China, India and Africa make general segregation quite impracticable at the present time, if only on account of the utterly prohibitive expense, so the successful Norwegian system cannot be applied to any large proportion of the world's lepers without the addition of some means of attracting the early cases and of dealing with them by some simpler, cheaper, and more effective method than life-long isolation.

Improved treatment as an aid to prophylaxis is the essential requirement, and in order to enable me to suggest a policy for reducing the incidence of leprosy I must here anticipate the main conclusions I shall come to in my next lecture regarding the present position of the improved treatment, which will then be fully dealt with, and may be summarised in the following statements:—

1. Early cases of leprosy are now coming forward voluntarily for the new treatment in Korea, the Philippines, Hawaii, India, and elsewhere in numbers formerly unknown.

2. Muir has now shown that the majority of these early cases are not infective, so may safely be treated in out-patient clinics at small cost, and that nearly all early cases lose their symptoms within a few months—the few bacteriological positive ones become negative and consequently no longer a danger to their households, while a fair proportion of later cases also clear up under prolonged treatment.

3. When a considerable proportion of the early cases can be thus cleared up, and members of their households examined repeatedly to detect and treat, on its first appearance, those developing the disease, the number of foci of infection in the houses will rapidly be reduced and the occurrence of new cases and the incidence of the disease will steadily fall.

By combining this new and hopeful measure with the isolation of as many as possible of the more advanced infective cases in special hospitals, sanatoria on the lines of tuberculosis hospitals, and colonies with land to cultivate and with the provision of the best treatment, a far more rapid decrease of leprosy will be brought about than ever previously possible. The Honolulu results of the last three years, which I shall deal with in my next lecture, indicate that, if they are maintained for another seven years, the total number of known



lepers in those islands will be reduced by nearly one-half within a single decade, or three times as rapidly as under the successful segregation system in Norway.

#### THE PRINCIPLES OF MODERN LEPROSY PROPHYLAXIS

The best prophylactic measures to adopt, necessarily vary widely under the conditions prevailing in different countries and climates, so that only the general principles can be laid down; these can most conveniently be considered first as regards areas in which compulsory segregation is adopted with a view to rapid reduction of the disease, and secondly, as regards the measures which are possible where compulsory methods are impracticable.

*Legalised Compulsory Measures Should Include :—*

1. Compulsory notification of lepers by both medical men and laymen under penalties, as recommended by the Paris Academy of Medicine in 1914, and enforced in Sweden, Iceland, the United States and some of our West Indian Colonies.

2. Examination and admission to institutions of the lepers by an expert medical board, which should also deal with cases recommended by the institution authorities for release as no longer infective, as in Honolulu and the Carville leper colony of the United States.

3. Compulsory isolation, with the provision of the best treatment available, as laid down in a resolution of the 1923 Strasbourg International Leprosy Congress, and retention until the patient is proved by repeated bacteriological examinations to be free from all infectivity, any released cases being examined at fixed intervals for several years, to detect and deal with possible relapses, as in the United States, Hawaii and the Philippines.

4. The examination of all household contacts of discovered lepers, about every six months for from three to five years, to detect new infections in the earliest and most curable stage of the disease. These periods are based on the results I have recorded of a study of 84 collected cases indicating an average incubation period of two to three years, while in 65 per cent. the time did not exceed three years and in 81 per cent. was not over five years; these figures show that four-fifths of new infections would be detected within the longer period.

5. The separation of the children of lepers from their parents as soon after birth as possible, and the prohibition of healthy children and adolescents from living in the same house with a leper, as in Iceland, where an unusually rapid decrease of leprosy has recently taken place. The prohibition of leper children or teachers in schools for healthy children is also essential, but has frequently been neglected.

6. The separation of the sexes in leper institutions, except husbands and wives beyond the child-bearing period, as enforced in Australia and the United States, the neglect of which measure in Hawaii and formerly in the Philippines, as already mentioned, led to infection of a large proportion of the children born to the lepers. In Panama an effective compromise has been adopted, worthy of imitation where complete separation of the sexes has not been found practicable, by only permitting marriages when the male leper applies for and submits to the simple operation of sterilisation by bilateral section of the vas deferens, which does not affect marital relationship, while preventing the procreation of children. The Calcutta Leprosy Conference of 1921 urged separation of the sexes to prevent the calamity of a healthy partner becoming infected while the other was recovering under treatment.

7. Countries adopting such stringent measures to eradicate leprosy must have legal powers to protect themselves from re-infection by repatriating all immigrants arriving with or developing leprosy within the longest known incubation period, which in exceptional cases has been known to extend to twenty or more years.

8. The prohibition of lepers from engaging in dangerous occupations, such as the preparation or sale of foods, clothing, cigars or cigarettes, the care of children or sick, domestic employment, midwifery, the barber's trade, prostitution, etc., is essential in all leprosy countries, although not yet enforced even in India.

Home isolation was permitted in Norway, mainly in the less infective nerve forms, where the accommodation permitted the leper being provided with separate room, cooking and table service, bedding, clothing, washing, etc., under close medical supervision; but this measure failed to prevent infections in Roumania and South Africa, and should not, in my opinion, be permitted when

there are any children in the house or when the case is an infective nodular one.

The treatment of early uninfected cases, in which no lepra bacilli can be found by repeated examination in the skin or nasal mucous membrane, as out-patients in special hospital or dispensary clinics, which Muir is rightly advocating as the most practical measure in such countries as India, where compulsory segregation is impossible, may also have to be considered where compulsory methods are enforced, and this measure appears to be worthy of trial to attract the early more amenable cases, with the proviso that any patients not regularly attending until released by an experienced medical officer will be liable to be segregated.

*Prophylaxis where Compulsory Segregation is Impracticable.* It will be remembered that in the early years of the Norwegian work, and throughout the successful campaign in Sweden, many lepers were isolated on a voluntary basis by supplying good hospital accommodation for them. Now that a far more effective treatment is already attracting many earlier cases of leprosy to hospitals, much more can be done towards isolating lepers on a voluntary basis than formerly, and the measures best suited to extend this policy remain to be considered; the following system has been advised by the Calcutta Conference and endorsed by the Government of India, and is gradually being brought into operation in the different provinces as funds permit.

*Leper Asylums and Colonies in India.* At present there are some 9,000 lepers segregated in India, some of the large cities having prison-like asylums with high walls surrounding small spaces, but most of the cases are in country asylums administered by the Mission to Lepers and other missionary bodies, with financial assistance from the Government, ranging from the well-organised Purulia institution with 700 lepers and ample ground for cultivation, to a small house with ten or so lepers. Some three-fourths of the inmates are advanced anaesthetic mutilated cases, for the most part uninfected and quite unamenable to treatment, whose isolation has little or no prophylactic value, while, unfortunately, in many of the asylums regular up-to-date treatment is not yet available.

Under the new system now being introduced, large institutions are being provided with ample land for cultivation, work on which



is as beneficial to lepers as exercise is for the tuberculous, and will also enable most of the required food to be home grown. Only infective cases should be admitted, under an efficient administrative and medical staff providing the best treatment and care, hospital accommodation for advanced and complicated cases, and a separate area, on a cottage or other convenient system, for the earlier ones to save them being repelled by the mutilated class, and another separate part for healthy children, the sexes being separated on the lines already mentioned. Patients becoming bacteriologically negative should be kept in a convalescent section until passed for discharge as at Carville, or separate small colonies with land provided for them as at Purulia, where there is already a village of recovered lepers, something on the lines of the Papworth tuberculosis colony near Cambridge.

These leper colonies, or, as they might well be called, sanatoria, will be complementary to the hospital and dispensary clinics already mentioned, as any advanced cases unsuitable for treatment at the latter, and likely to repel the attendance of the early amenable class it is so important to attract, should be sent to the colonies for prolonged treatment and care. Where the clinics are opened before colonies are available, the difficulty may be dealt with by arranging for the early cases to attend on different days from the more advanced and infective ones.

As the proposed well-equipped and staffed colonies will be expensive institutions to maintain, I regard it as most essential that advanced mutilated, little or not infective, begging anaesthetic cases should not be admitted to them, as treatment will be useless, and its apparent failure depressing to the more amenable nodular cases, while it is a waste of good money to isolate cases who are no danger to the community, and should be looked after by their relatives. The good example of South Africa in releasing from the asylums, the 693, or 28 per cent. of the total of such uninfected lepers is worthy of imitation in other countries without unlimited funds for dealing with leprosy.

In our tropical African colonies the difficulties of dealing with the leprosy problem are even greater than in India, although the same principles are applicable, beginning with the provision of leprosy clinics for treatment until the confidence of the patients is gained,



when the more infective cases may be induced to live in leper villages, which are already a familiar measure among many tribes. Sir Hugh Clifford, in Nigeria, has started some leper villages into which only lepers are admitted, allowing them to retain their self-respect, while all children born to them are removed from danger of infection by being sent to healthy relatives as soon after birth as possible: an admirable system which is worthy of wide adoption under similar circumstances.

Such, in brief outline, are the conclusions I have come to on the vexed question of leprosy prophylaxis based on three years' minute study of the literature, and adapted to take full advantage of all the recent advances in our knowledge of the epidemiology and treatment of this terrible disease. Many decades of patient work lie before us, but I feel it is high time we made a serious attempt to utilise the means we now possess of reducing leprosy in our Empire; regarding which our American cousins have recently set us such a good example in Hawaii and the Philippines.

### Lecture III. THE TREATMENT OF LEPROSY

*Preliminary Considerations.* Leprosy presents many difficulties in estimating the effects of any given treatment, due to differences in the types of the disease, the very chronic and variable course it runs with sudden exacerbations, sometimes followed by temporary improvement. Moreover, in the anaesthetic variety there is a tendency for the progress of the disease to cease and even for the infection to die out, although rarely until after serious permanent crippling of the extremities has been produced through nerve destruction rendering treatment ineffective. On the other hand, when ill-nourished begging lepers are cared for in an asylum, considerable improvement may ensue without drug treatment; for which reasons short trials of drugs in a few cases have little value. Even more difficult is the estimation whether great improvement, even amounting to disappearance of all active signs and infectivity of the disease under prolonged treatment, will prove permanent or not: the analogy with tuberculosis being here very close, for it is impossible to say whether any living bacilli which may produce a relapse some years later remain quiescent in the tissues. The spontaneous

disappearance of very limited anaesthetic patches has also very occasionally been met with, but natural recoveries of the nodular forms rarely if ever occur, although such cases may sometimes develop nerve symptoms, which gradually predominate over the skin ones, forming mixed cases of leprosy. In short, there is a nicely balanced struggle between the invading bacilli and the tissues of their host, liable occasionally to be turned in favour of the latter, which necessitates caution in judging of the effects of any remedy without long observation on a series of cases, but which also affords good hope of curative measures being discovered by patient research. These now appear to be within sight in certain soluble derivatives of chaulmoogra and other oils, before dealing with which a brief review of other methods which have afforded great temporary improvement and a few apparent cures will be of interest and throw some light on the conditions favouring recovery.

*Mineral Preparations.* Mercurial preparations have been recommended from the days of Pjetursson in Iceland, in 1769, to Radcliffe Crocker in 1896, but have not recently met with favour. Arsenic was advised by Danielssen in Norway, while atoxyl, arrhenal, salvarsan and, recently, eparsono have been advocated, chiefly by French writers, with variable and uncertain results. Antimony intravenously has recently been advised by F. W. Cawston, and appears to be of some value in healing leprotic ulcers, although workers in Culion and elsewhere have not been able to confirm the original claims made for this form of medication. Cyanocuprol has been advised in both tuberculosis and leprosy by Japanese workers.

*Iodine* has greater claims; Danielssen in 1886, and others, using the iodide in the treatment and diagnosis of leprosy, observed febrile and local reactions in nodular lesions, with the disappearance of old and the appearance of new nodules, as well as increased discharge of lepra bacilli in the nasal mucus of diagnostic value following its use. Iodoform and eucophene injections have been advised by Neisser and others, while Clegg and Hollmann obtained interesting febrile reactions after the inhalation of 15 to 30 minims of ethyl iodide, and Marchoux and Bourret in 1909 observed that during reactions following iodides, large numbers of leprosy bacilli lose their acid-fastness and are destroyed; so the drug may be of

value in conjunction with other remedies, although by itself it has failed to produce lasting beneficial results in leprosy. Ichthyol, guaiacol, strychnine, etc., have also had their advocates.

*Local treatment* has been advocated, especially by G. Unna, including the destroying of nodules by shaving off with a razor, applying carbolic acid, hydrochloric acid, caustic potash, the cautery, etc., but the claims to eradicate the disease in early cases by such measures have not been substantiated. Tincture of iodine, carbon dioxide snow, ethyl chloride (Lie), trichloroacetic acid, mineral baths, X-rays, radium and electric currents have all had their advocates: the multiplicity of remedies indicating that no really satisfactory one was available up to very recent times.

*Serums* against leprosy have been prepared by Carrasquilla in Colombia, in 1896, by injecting horses with the blood of lepers, while later others, with more reason, but without success, injected animals with antigens composed of juice of nodules, containing lepra bacilli while Dyer in America tried antivenomous and normal horse sera with no result.

*Vaccines* made from various acid-fast organisms have been extensively tried with temporary good results in some cases. Tuberculin produces well-marked reactions in leprosy, but with large doses of Koch's original form more harm than good was done, an analysis of fourteen papers up to 1892 showing that slight improvement was only claimed in one trial, but in 1896 Arnaud saw disappearance of nodules and improvement continuing for two years following a severe reaction: a case that once more illustrates the great benefit occasionally following upon violent reactions induced by very different lines of treatment. In 1904-5 Lie of Norway recorded post-mortem evidence to prove that reactions may be obtained with tuberculin injections in lepers who were quite free from lesions due to the tubercle bacillus, but he failed to get benefit in lepers he treated with small doses of tuberculin, although in 1909 Baber reported remarkable improvement in several cases after the use of tuberculin combined with chaulmoogra oil.

Nastin is essentially another non-specific vaccine made by Deycke by dissolving a fatty substance, extracted by ether from an acid-fast streptothrix, in benzoyl chloride, the injection of which, in leprosy, also produced febrile and local reactions, sometimes



followed by considerable improvement, very promising results being reported for a time by Deycke and others, until a four years' trial in British Guiana, initiated by the discoverer himself, and reported on by Wise and Minett in 1912, showed that general reactions with softening and absorption of the nodules only occurred in 3.5 per cent., of the cases treated and in the remainder early slight general improvement during the first three months was followed by retrogression, and the patients got steadily worse; their conclusion from prolonged study of 244 unselected cases was that nastin produced only 'a slight temporary check during the first six months of treatment, but otherwise the natural course of leprosy continued unchanged.' Such temporary changes accounted for the improvements shown in Deycke's tables, while subsequently Minett found that injections of benzoyl chloride alone produced precisely the same effects as Deycke's nastin-B itself.

Vaccines from supposed acid-fast bacilli of leprosy have been made by Rost, Williams, Clegg and others from cultures obtained from cases of leprosy, which, however, Walker has recently shown cannot be distinguished from the smegma bacillus, so are also non-specific acid-fast bacilli, but their use has undoubtedly been followed by local and general reactions, as with tuberculin, followed in some cases by great improvement, only too often of a temporary nature. Harm, however, can also result; Rutherford, in twenty carefully noted cases, found that the deterioration exceeded the improvement, while Clegg's bacillus gave negative results in Honolulu: the effects of this treatment on the whole are, therefore, disappointing.

Vaccines made from excised lepra nodules, containing enormous numbers of lepra bacilli, have also produced some benefit, but this plan has obvious limitations, especially where the disease is not common. Nevertheless, as will appear presently, the reactions produced by the various acid-fast bacillary vaccines may make them of some value in combination with other lines of treatment.

*Chaulmoogra oil* is an old Indian remedy, which one writer thinks was referred to in the ancient writings of Susruta as 'tuvaraka,' but was introduced to western medicine by Mouat in a paper in Vol. I of the *Indian Annals of Medical Science* of 1853-4, and was made official in the Pharmacopoeia of India in 1868 and in the Indian



and Colonial addendum to the British Pharmacopeia in 1901. There has been a good deal of confusion regarding the origin of the oil, which was for many years erroneously described as being derived from the seeds of *Gynocardia odorata*, until in 1901 Sir David Prain showed that it came from those of *Taraktogenos kurzii* (King) growing along the banks of the rivers of Assam, Chittagong and Burma. It has since been found that various species of *Hydnocarpus*, the most important of which are *H. wightiana* of Southern and Western India, and *H. anthelmintica* of Siam, Indo-China and China, all contain the same active unsaturated fatty acids as *Taraktogenos*, so that it will be convenient to include the oils of both these genera, but not that of *Gynocardia odorata*, under the term chaulmoogra oil.

Much work has been done on the chemical constitution of these oils, Moss, as early as 1879, separating the lower melting point acids under the term gynocardic acid, while Power and Gornall in 1904 and the following years separated first the highest melting point (68° C.) chaulmoogric acid, established its chemical formula and made a number of compounds, including methyl and ethyl chaulmoogrates, and in 1905 Power and Barrowcliff isolated from *H. wightiana* oil, both chaulmoogric and a lower melting point acid (60° C.), named by them hydnocarpic acid, all of which I shall have to refer to again.

Chaulmoogra oil taken orally has long had a reputation in the treatment of leprosy, but has the great disadvantage of being so nauseating that few patients can take sufficient to do more than retard the progress of the disease. The best results have been obtained by Ralph Hopkins, with fifteen years' patient work in the Louisiana Hospital, with 30 per cent. improved, 5 per cent. progressed and 71 per cent. died, of 88 advanced cases; 17 per cent. cured, 4 per cent. lesions disappeared, 48 per cent. improved, 5 per cent. progressed and 12 per cent. died, of 82 incipient cases, showing that only in incipient cases was very material benefit obtained, but demonstrating that the oil had a definite value in leprosy.

A Chinese method of giving the fresh *Taraktogenos kurzii* nuts orally combined with hemp and another Chinese drug has recently been reported by E. A. O. Travers of the Kuala Lumpur Leper Asylum in the Malay States, to have cleared up the symptoms of a certain number of cases of leprosy, while the nuts are very

cheap and readily taken by women and children. He is now, at my suggestion, trying *Hydnocarpus wightiana* nuts, for Reed states that these keep fresh for months if dried, and they can be obtained at about three shillings for 80-lbs. weight, from the Ernakalum Trading Co. of Southern India, being much easier to get than those of *Taraktogenos*. Competent botanists assure me that the *Hydnocarpus wightiana* tree is likely to grow well in any hot, moist climate, with a good rainfall, that is in just those districts where leprosy is so common, and I hope to be able to get the seeds of this species widely distributed before long, if the Malay results are confirmed by further experience.

The importance of the above methods of administration is that they have led to the discovery of more efficient preparations derived from the oils, the evolution of which must now be described.

Gynocardic acid, consisting of the lower melting point fatty acids of the oil, has been used orally since 1891, together with sodium and magnesium gynocardates, with apparent benefit in some cases. I administered gynocardic acid to a few lepers during the first decade of the present century, and came to the conclusion that it was much less irritating to the stomach and more effective than the whole oil, one European patient taking up to forty grains a day for a year, with the result that a very extensive macular leprosy completely cleared up, although some nerve symptoms persisted. As early as 1912 I asked an important firm of manufacturing chemists if they could make for me some soluble compound of gynocardic acid suitable for injection, but unfortunately received a reply in the negative.

In 1911 Engel-Bey reported good results in a few lepers treated orally in Egypt with antileprol, made at his suggestion by separating the free acids of chaulmoogra oil and esterising them, while in 1913 H. Bayon gave this preparation both orally and intramuscularly.

Chaulmoogra oil intramuscularly appears to have first been used successfully by Tourtoules in Egypt, who reported apparent recovery in one case after 650 injections totalling 2,720 grammes in the course of six years, ending in 1899, while Hallopeau in Paris reported benefit in nine lepers treated with combined oral and intramuscular administration, although Castel in 1899 recorded pulmonary embolism in two cases. Jeanselme in 1911 injected

a mixture of chaulmoogra oil, camphor and guaiacol, while in 1914 Victor G. Heiser reported from the Philippines 11 per cent. of apparent cures in a small series of cases treated for prolonged periods by intramuscular injections of a mixture of equal parts of chaulmoogra oil, camphorated oil and resorcin, and later Hopkins, McCoy and Hollmann recorded successes by this method, which thus constitutes an important advance.

*Sodium Gynocardate Intramuscularly and Intravenously.* As the result of Heiser's success with chaulmoogra oil intramuscularly, and of a personal visit from him in Calcutta in 1916, I renewed my attempts to obtain the active portion of the oil in a soluble form suitable for injection, and with the help of Dr. Chuni L. Bose, Professor of Chemistry, and later of the whole time assistance of Dr. Sudhamoy Ghosh, D.Sc., Edin., and with the financial assistance of the Indian Research Association, I obtained first sodium gynocardate, and subsequently similar compounds of the various fatty acids of chaulmoogra, cod-liver and other oils, and investigated their action in numerous cases of leprosy during the next four and a half years. The following results were obtained:—

Intramuscularly sodium gynocardate, prepared from gynocardic acid with a melting point of  $37^{\circ}\text{C}$ ., was better borne by Indian patients than the whole oil, and although it produced local pain and induration it gave promising results. I next ascertained by animal experiment that it could safely and practically painlessly be injected intravenously with only very temporary giddiness in a 3 per cent. solution, a large medio-basilar vein allowing of weekly injections for upwards of a year, but when only small veins were available, as is often the case in women and children, irritation of the inner lining of the vein at the immediate site of injection might produce strictly localised and harmless obliterative phlebitis limiting the injections; this irritation was only partially prevented by the addition of  $\frac{1}{2}$  per cent. sodium citrate to the solution. I next found that the sodium salts of chaulmoogra oil, fatty acids with melting points of from  $49^{\circ}$  to  $51^{\circ}\text{C}$ ., containing both gynocardic and hydnocarpic acids, and which I called gynocardate of soda A, were more effective in leprosy than those of the lower melting point acids, while the salts of chaulmoogric acid itself were much less soluble and also less active. Eventually I came to the conclusion



that the salts of the whole of the fatty acids of *Hydnocarpus wightiana* oil, containing more hydnocarpic and less chaulmoogric acid than the oil of *Taraktogenos kurzii*, gave the best results, and this oil has since been used in Calcutta by Muir and by many other workers in the East in making preparations for injections in leprosy, the tedious and expensive process of fractionation being unnecessary now that these points have been established by careful investigations. Professor B. E. Reed of the Peking Union Medical College, has recently stated that *Hydnocarpus* preparations, mainly supplied from Calcutta, have found favour in Singapore, the Malay States, Burma and elsewhere, and he concluded that 'the antiquity of the records of *hydnocarpus*, the continuity of its use in many countries, its high chemical and therapeutic worth, give it a place of international importance.'

*Reactions with Destruction of the Lepra Bacilli due to Gynocardates and Hydnocarpates.* The subcutaneous injections of sodium gynocardate produced gradual improvement in leprosy cases, without the occurrence of any marked reactions in the affected tissues, but when I commenced to give the preparation intravenously a remarkable and hopeful phenomenon was observed, nearly always in rather advanced nodular cases with enormous numbers of lepra bacilli in the affected tissues. The reaction which took place is well illustrated by a coloured plate I published in 1919 showing inflammatory swelling and softening of the leprosy infiltrated lobes of both ears, while microscopical examinations of excised portions in such cases revealed only a few remaining typical rod-shaped acid-fast bacilli, together with innumerable acid-fast granules of disintegrated organisms, demonstrating that the inflammatory local reactions produced by this vegetable substance had resulted in the destruction within the human tissues of enormous numbers of the pathogenic organism, and opening up possibilities of an important advance in the treatment of this hitherto intractable disease. Fever for a day or two always accompanies such reactions, which may be induced by very minute doses of the drug, and very occasionally fever may persist for one or more months. This is accompanied by a softening of numerous nodules and a considerable degree of toxæmia resulting in prolonged debility, while a number of new skin lesions may appear in the form of slightly



raised red patches, just as occurs naturally, from time to time, in the more acute cases of nodular leprosy in what Muir calls the reactionary phase of untreated cases. As few bacilli are found in reaction lesions they may largely be due to inflammatory reactions excited in small deposits of lepra bacilli, which had not previously produced visible lesions while still quiescent. As a rule such reactionary lesions appearing during treatment clear up again rapidly, although occasionally some of them persist and the patient appears to be worse for a time, so it is now generally considered advisable to try as far as possible to avoid the more severe reactions by cautious dosage in the active second stage of the disease. Muir, however, finds that in the first stage of very limited lesions, as well as in the third quiescent stage, when the reactionary phase no longer occurs naturally owing to the establishment of tissue resistance to the toxins of the bacillus, the treatment may safely be pushed with beneficial effects. Considerable experience, both as regards the natural course of the different varieties of leprosy and also in the exhibition of the powerful remedies now available, is thus necessary to enable the best results to be obtained, which is, doubtless, the reason why some observers have failed to get good effects in their earlier attempts to use the new treatment.

Severe febrile and local reactions are, however, exceptional, steady improvement in their absence far more frequently ensuing, although careful observations in the wards of leper institutions enabled Muir to observe that slight rises of temperature, not noticed by the patient, nearly always occur in patients showing fairly extensive bacteriologically positive lesions, indicating the destruction of smaller numbers of bacilli of a beneficial nature. I was also able to demonstrate by repeated microscopical examination of small excised portions of nodules from the ear or other affected part, that in the entire absence of any reactions noticeable to the patient a gradual breaking up and diminution of the lepra bacilli was brought about by repeated injections of these preparations, accompanied by slow absorption of the nodules, until nothing but a few acid-fast granules could be detected; this stage, in turn, was soon followed by the entire disappearance of the bacilli from the tissues, as well as from the nasal mucus, rendering the patients apparently free from both all the symptoms and infectivity of the disease,

six to eighteen months usually being required to bring about this happy result in typical, but not extremely advanced, nodular cases.

In anaesthetic cases with nodular thickening of the ulnar nerves, I have also seen reactions consisting of temporary swelling of the nodules accompanied by severe pain, sometimes necessitating the use of morphine, but followed by subsidence and eventual great improvement of sensation in the area supplied by the affected nerve, while in less advanced cases steady, but usually slow, return of both sensation and muscular power occurred, together with eventual disappearance of the depigmented patches in various parts of the body. One of the earliest cases of this type, with foot drop greatly crippling him, lost all visible signs of the disease and became able to walk ten miles at a stretch. On the other hand, when nerve trunks of the extremities have been extensively destroyed by prolonged disease, and fingers and toes have been lost, or the typical claw hand with wasting of nearly all the intrinsic muscles has developed, complete restoration of function is obviously impossible, although a considerable degree of recovery of sensation and muscular power may take place when the disabilities are of recent origin, but not in the long standing crippled cases, so frequently seen in Indian leper asylums, with permanent destruction of extensive portions of their distal nerve trunks by irremovable fibrous scar tissue. Such wrecks of humanity may remain in a stationary condition for several decades before some intercurrent disease releases them from their misery, and the disease can only be prevented from reaching this incurable stage by effective treatment at an early period.

An even more remarkable and important phenomenon which I have observed in a very few bad nodular cases, who developed most prolonged and severe febrile reactions after even a single minute dose of sodium gynocardate, with great debility and inflammatory softening of extensive lesions, has been a steady improvement extending over many months, without any further treatment, and even complete recovery during the ensuing year; of this type of case the following are examples: One of the worst cases I have seen of nodular leprosy of twenty years' duration, with extreme thickening of the skin of the face and extensive ulceration of both the ears and

the hands, had three months fever after the minute intravenous dose of 0.2 c.c. of a 3 per cent. solution of sodium gynocardate, followed by steady improvement without any further treatment, and at the end of a year only loose folds of skin remained at the site of the former facial nodules, and the ears and hands had completely healed. Another patient with a 'grog blossom-like' nose and raised red leprotic patches the size of the palms of the hands on his body, after two months reactionary fever following a few small doses of the same drug with great loss of strength, was given no further treatment except sodium morrhuate orally, although he was anxious to continue the injections. I sent him away for a change as soon as he began to pick up, and saw him again about a year after the reaction, when only slight pitting with some fibrous scarring remained at the sites of the former extensive lesions, sections of removed portions being quite free from acid-fast bacilli; complete recovery had thus taken place. Such cases are quite exceptional, but their occurrence at least indicates that the action of chaulmoogra oil soluble preparations cannot be explained solely by any direct destructive effect on the lepra bacilli: a point of great theoretical importance which I shall return to in the last lecture.

*Sodium Morrhuate and Sodium Soyate in Leprosy.* The destruction of the lepra bacillus after intravenous injections of gynocardates naturally led me to consider the possibility of inducing a similar change in the acid-fast bacillus of tuberculosis, and I consequently got Dr. S. Ghosh to extract the fatty acids from cod-liver oil and make a sodium salt for me, which I called sodium morrhuate. I found it made a clear solution almost unirritating both by subcutaneous and intravenous injection, so I next tried it by both methods in leprosy, and soon observed that it could induce by either mode of administration febrile reactions in leprotic tissues with destruction of the lepra bacillus, followed by similar improvement and ultimate disappearance of all signs of the disease. This will be evident from the coloured drawing I show you, in which six months' treatment with practically painless subcutaneous injections of a 3 per cent. solution of sodium morrhuate brought about the absorption of very numerous raised circinate red patches on all parts of the body of the patient, with disappearance of the lepra bacilli, leaving only lighter depigmented patches, although it should be



mentioned that he left off treatment against advice at this stage and I found a slight recurrence in one spot a year later.

As the value of chaulmoogra oil had previously been attributed to its possessing a closed carbon ring, a unique constitution for a fatty acid, the activity of sodium morrhuate in leprosy disproved that interesting theory, and led me to think that the proportion of unsaturated fatty acids as a class might be the most important factor influencing the therapeutic value of oils in leprosy. To test this theory I next selected some oils with a high iodine value, including soya bean oil and Japanese sardine oil, and had similar sodium salts of their unsaturated fatty acids prepared; I found the latter to be irritating to human tissues, but the former, which I called sodium soyate, formed a clear and unirritating 3 per cent. solution suitable for injection either subcutaneously or intravenously. There was only time to try it in a few cases before I left India, in one of which an extensive, red, raised leprotic patch covering the whole of one cheek, together with smaller ones on other parts of the body, completely disappeared and the tissues became bacteriologically negative in the remarkably short period of six weeks; this is by far the most rapid improvement I ever saw in a case of that degree, although the effects were much less rapid in the other cases, and as far as I know, this preparation has not since been tried on a sufficient scale to decide its precise value. The few tests I did, add yet another oil to those furnishing active preparations against the acid-fast bacillus of leprosy. In 1919, Dr. K. K. Chaterji, of Calcutta, applied my methods to nim oil, and reported great benefit in two lepers treated by 'margosates' thus prepared. During the last two years, Muir has obtained active preparations on the same lines from linseed and olive oils, although he concluded that those prepared from the 'closed ring' fatty acids of chaulmoogra oil were rather more effective in leprosy than the others, while preparations from saturated fatty acids had very little effect in this disease. This largely confirms my theory, and at the same time opens up an unlimited field of research on the many oils, which may furnish still more effective preparations, both in leprosy, and possibly also in tuberculosis.

*Results of Treatment with Gynocardates and Hydnocardates and with Sodium Morrhuate.* In 1917, I reported twenty-six leprosy cases



treated for three or more months with sodium gynocardates and hydnocarpates with improvement in all, while eight of the twelve treated for a year or more had lost all signs of the disease, and added 'whether permanent results can be obtained only time will reveal.' In 1919, I recorded fourteen cases treated with sodium morrhuate, and the following table shows the results obtained in all the cases I had treated for three months and over, when I left India early in 1920, the sodium morrhuate series being shown separately.

TABLE III

	Not Improved	Slightly Improved	Greatly Improved	Lesions all disappeared	Total Cases
Gynocardates and Hydnocarpates— 3 months and over ... ..	1	9	20	21	51
Gynocardates and Hydnocarpates— over 1 year ... ..	1	1	2	9	13
Sodium morrhuate— 3 to 12 months ... ..	0	3	12	5	20

Thus, with the chaulmoogra oil preparations, in round numbers, 40 per cent. had cleared up completely and another 40 per cent. had so greatly improved that there was very good probability of their losing all signs of the disease with further treatment, giving 80 per cent. of good results, while of 13 cases treated for the sufficient period of a year or more, 9, or 69 per cent., had cleared up completely. The sodium morrhuate cases had been treated for shorter periods of from three months to one year and of 20 cases 12 had greatly improved and 5 had completely cleared up, the results being about equal to those with the gynocardates and hydnocarpates when the duration of treatment is taken into account. In only one very advanced nodular case of the total 71 cases had no improvement resulted, but it must be mentioned that as the cases represented all stages of leprosy, including some early ones, they were considerably more favourable than the average type met with in leper asylums.

As I pointed out in 1919, relapses occur in some cases which leave off the treatment as soon as the lesions have disappeared, and of 34 cases followed up since my report of 1917, one remained unimproved, 10 had further improved under continued treatment, in 5 the lesions

had now disappeared, 13 remained clear of symptoms and 5 had relapsed—the latter, all cases in Indians who had left off the treatment prematurely against my advice. These results clearly indicate the necessity of continuing injections for some months, or better still a year, after the disappearance of outward signs of the disease, as was only to be expected in a chronic affection due to a highly-resistant organism. Some of the relapsing cases cleared up again on resuming treatment. Further cases becoming stationary on hydnocarpate treatment, may proceed to clear up completely on using sodium morrhuate, illustrating the advantage of having more than one effective remedy.

*Disadvantages of the Intravenous Method.* The necessity of giving sodium hydnocarpate intravenously to obtain the best results is a serious disadvantage, on account of its irritant action on the veins, leading to obliteration, and the time consumed as compared with an intramuscular injection. Further, sodium morrhuate has been found to deteriorate in solution through oxidation, while it is troublesome and expensive to put it up in capsules to avoid change. Dr. Ghosh made some ethyl hydnocarpate for me, which I had not the time to try to any extent before I left India, and the next advance is due to American workers.

*Ethyl Ester Chaulmoogrates Intramuscularly.* In 1919 Dr. H. T. Hollmann and Professor Dean of Honolulu reported on the use of intramuscular injections of ethyl esters of the different fractions of the fatty acids of chaulmoogra oil, and confirmed my conclusion that the chaulmoogric acid fraction produced little effect, but that the lower melting point ones were more active. They obtained marked improvement in 17 out of 26 cases, improvement in 3, slight improvement in one and no improvement in 3, who had been treated for three months or less, very similar results to my earlier Calcutta ones. Their method had the great practical advantage that the ethyl ester could be injected in a pure fluid state into the gluteal muscles without much pain, enabling a large number of cases to be dealt with in a comparatively short time. This convenient modification has since been very generally adopted in many parts of the world with slight variations, Muir having introduced a very convenient formula, which in its latest form consists of equal parts of ethyl hydnocarpate (prepared from *H. wightiana*) and of pure olive oil,

with 4 per cent. double distilled creosote (E.C.O. mixture), his former E.C.C.O. mixture having also contained camphor (which J. G. Samson and G. Limkako at Cullion found to be useless, although they confirmed the value of the addition of creosote), or 10 per cent. thymol (E.T.O.) may be substituted for the creosote. Muir advises injections of these mixtures either beneath the leprous lesions or intragluteally, or both, in doses rising by 0.5 c.c. at a time from 0.5 c.c. up to a maximum of 10 c.c. once or twice a week, the next dose being reduced if the temperature rises to 100°F. and remains up for more than 24 hours, while if any marked reaction occurs in the diseased tissue, injections should be stopped until it has completely subsided.

At my suggestion Muir tried giving iodide of potassium orally in daily doses of from  $\frac{1}{2}$  to 20 grains, and found this addition may induce reactions after ethyl hydnocarpate when absent without it, resulting in further improvement, and he has also used a vaccine of Kedrowsky's acid-fast bacillus with success for the same purpose : illustrating the principle that a variety of substances, that I showed in the historical review of former treatments have produced reactions in leprosy, may be of value to supplement the action of the new methods. Time does not permit me to go into further detail regarding the treatment of different stages of leprosy, which will be dealt with in a work on which Dr. Muir and I have been long engaged, and I must pass on to consider the results which have been obtained in other countries where the different remedies have been tested, the most extensive trials of which we owe to American workers.

In India I arranged, through the kindness of the Mission to lepers, for a trial of both sodium gynocardate and sodium morrhuate separately in thirteen leper asylums, and asked Dr. Muir to make an independent analysis of the results. 300 cases showed 72 per cent. improved and 32 per cent. greatly improved although the treatment had only lasted for from two to twelve months, and those treated for six months and over to a year gave 100 per cent. improved and 52 per cent. greatly improved, the more promising cases having been selected for treatment, while the two preparations gave almost identically the same results, establishing the principle that those from other oils than chaulmoogra may be effective in leprosy.

*Results with Ethyl Chaulmoogrates and Hydnocarpates.* It is still too early to allow of anything like final conclusions regarding the precise value of the new treatment in leprosy, but the following extensive trials will afford some indications. During the last two years a great test was begun in the Culsion settlement under Dr. H. W. Wade, who has kindly sent me a preliminary report showing that treatment was begun first in May, 1921, 500 cases being treated during the next two months, and gradually increased to 1,500 by April, 1922, and 4,067 in the following year. A survey in September, 1923, showed improvement in 55.9 per cent., while in 36 per cent. more the progress of the disease had been checked, 6.4 per cent. were worse, and 1.7 per cent. had died, and concluded that under the circumstances 'it is felt that this result is far from discouraging.' This opinion is strengthened by the following figures which speak for themselves, showing the percentages improved after different periods of treatment.

MONTHS OF TREATMENT ...	Under 3	3-6	6-9	9-12	12-15
PERCENTAGE IMPROVED ...	26 %	42 %	74 %	81 %	93 %

In HAWAII still more instructive figures are now available on account of the much longer duration of the treatment by ethyl chaulmoogrates at the Kahili hospital near Honolulu, where all newly discovered lepers are first sent for diagnosis and treatment, and the most advanced unamenable ones eventually drafted on to the Molokai settlement. From 1912 to 1918, before the introduction of the new improved treatment, the yearly discharges on parole as recovered averaged 6.5, during the first two fiscal years ending on June 30th, 1919, and 1920, of the new treatment, 20 and 31, respectively, were thus discharged, in 1920-21 there were 115 new admissions and no less than 94 discharged recovered; of these 23 relapsed, so in 1921-22 under stricter rules only 26 were paroled, the number rising again the following year, 1922-23, to 52. During the last three years, when the full effects of the improved treatment were obtained, there were 310 admissions and 172 discharged recovered, or 55.5 per cent. of the number admitted during the same period, all after examination by a board of three experienced doctors; 16 died of complicating diseases, mostly from tuberculosis. During the last four years 92 cases were transferred to Molokai as not yielding to treatment, a yearly average of 22.3 per cent., or less than one-fourth of the average yearly admissions. Further, of a total



of 249 paroles in the ten years, 1912-21, 31, or 12.4 per cent. relapsed, some of whom cleared up again on further treatment.

To understand the full significance of these figures we must recall that the usual annual mortality among the advanced cases seen in leper asylums and settlements is rarely less than 10 per cent., and is often higher; the recent Hawaii admissions of the last three years show a diminution each year of about 10 per cent. on the numbers of the previous year, which it is not unreasonable to hope may continue, in view of the numbers of cases now being cleared up in the early stages before they have had the prolonged opportunities of infecting their households, as when they hid their disease in the absence of any efficient treatment, instead of declaring it voluntarily as so many have done recently. If such proves to be the case I estimate that the total known Hawaii lepers will decline by over 40 per cent. within one decade, or far more rapidly than has ever been known in a tropical country in the absence of any effective treatment: clearly illustrating the value of the new methods in the age-long struggle to stamp out leprosy.

The immense importance of treating leprosy in its early stages is proved by the following Honolulu figures of the percentages of recovered cases in relation to the duration of the disease on commencing treatment.

YEARS DURATION...	Under $\frac{1}{2}$	$\frac{1}{2}$ -1	1-2	2-3	3-4	4-5	5-8	8-10	Over 10
RECOVERED ...	44%	18.5%	17%	10.5%	9%	4%	4%	3%	9.5%

The much higher recovery rate in early cases is well shown by these figures, while in my own cases I found that 50 per cent. of cases treated within three years of the onset cleared up completely, but only 25 per cent. of those from three to fifteen years' duration did so. It is also of great significance that in Hawaii in former days the discharge as recovered scarcely ever occurred in the nodular type, while under the new treatment just over two-thirds of those released on parole were of this previously incurable form. The younger age groups also yielded the largest proportion of successes.

These results are also in accordance with Muir's recent statement: 'We have found, further, that most early cases lose all signs of active disease within a few months. . . . The most hopeful method of dealing with leprosy must, therefore, depend on early diagnosis and treatment.' Dr. Travers, who is now in charge of a leper asylum

in the Malay States after long service there, has recorded his opinion that 'if taken in time, the progress of the disease can be arrested and that in a large proportion of cases, leprosy can be actually cured.' Muir also states 'Our experience shows that leprosy can almost always be diagnosed long before it becomes infectious; that is to say, the disease may be recognised by clinical signs long before bacteriological examinations are positive,' and he rightly, in my opinion, advocates the multiplication of leprosy clinics, something on the lines of tuberculosis dispensaries in Britain, but with far brighter prospects of successfully eradicating the plague.

*Can Lasting Cures be Obtained?* It is now established that most early and some more advanced cases lose all symptoms and infectivity of leprosy under treatment, but it is still too early to say in what proportion of such cases the whole of the lepra bacilli have been destroyed with consequent permanent cure apart from reinfections. The frequency with which relapses occur in tuberculosis after apparent cure by sanatorium treatment necessitates the greatest caution in claiming permanent results in leprosy before sufficient time has elapsed to justify these claims. Nevertheless, the outlook even in this respect appears to me to be far more favourable than in tuberculosis, for one of my early patients has now remained free for over eight years from all signs of the disease, except for the crippling of one hand due to irreparable damage to an ulnar nerve, although he has had no treatment during the last three years; several more cases had remained free from all symptoms for five and six years when I last heard from them. In Hawaii 88 per cent. of the paroled cases have remained well for several years, and although it is advisable to continue some treatment for a year or so after apparent recovery, yet with this precaution there are now good grounds for hoping that the results will be permanent in a large proportion of the earlier cases at any rate. Moreover, the evidence that the treatment actually leads to destruction of the lepra bacillus in the body not only places it in a more hopeful position than the building up of the resisting powers of the tissues by the sanatorium treatment of tuberculosis, but also raises the still more important question of the possibility of applying the new line of treatment to the white man's scourge, tuberculosis.